HEMODYNAMICS

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Hemodynamics

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"For since we are assured that the animal fluids move by *hydraulic* and *hydrostatic* laws, the likeliest way therefore to succeed in our inquiries into the nature of their motions is by adapting our experiments to those laws."

Stephen Hales, *Haemastatics,* 1733

Preface

Hemodynamics is concerned with the forces generated by the heart and the resulting motion of blood through the cardiovascular system. It is at once a body of theory and an experimental science, to which physicists and mathematicians have contributed equally with physicians and physiologists. The elementary principles of hemodynamics are familiar to most students of physiology and medicine, but research workers, physicians, and others who make professional use of modern hemodynamic methods require a more extensive knowledge. The present volume is therefore an attempt to provide a comprehensive account of the subject, beginning where introductory texts generally leave off and leading up to questions that remain unanswered today. It is intended as a work of reference, keeping in mind the different needs of those whose training may have been in medicine, biology, or engineering. The diversity of this potential audience is natural in a field that crosses academic boundaries, where everyone must learn to be at home in more than one discipline.

Cardiovascular physiology in general, of which hemodynamics is but a small part, is discussed in this volume only where it bears directly on circulatory dynamics, and some familiarity with the basic facts of mammalian physiology is desirable. An elementary knowledge of calculus, trigonometry, and classic physics is also assumed, but most students will find that occasional reference to basic college texts is all that is necessary. Mathematics is an indispensable language for the expression of hemodynamic concepts, affording both clarity and precision, but virtually all the essential ideas are also presented verbally. Readers approaching this subject for the first time should not hesitate to skip most of the derivations and concentrate instead on the qualitative relationships stated in the equations. The importance of hemodynamics does not lie in its mathematical or theoretical results, of course, but in their application to physiological research and medicine. Clinical applications are at an early stage, but their success has already been amply demonstrated. To give but two examples, they have made it possible to examine arterial elasticity in health and disease and have led to the investigation of shearing stresses as a possible factor in the etiology of arteriosclerosis.

My debt to the late Donald A. McDonald will be evident to everyone familiar with his classic work, *Blood Flow in Arteries,* which first appeared in 1960. That monograph, and the revised edition in 1974, brought into perspective the long history of theoretic and experimental work in the subject, including the important contributions made by McDonald and his associates. The present volume brings many of the same topics up to date, but it is also intended to cover the field more broadly, and to meet the needs of students at all levels. The colleagues with whom I have worked at various times have contributed immeasurably to my education and it is a particular pleasure to acknowledge my indebtedness to Dr. Derek H. Bergel, now at Oxford University, and Dr. Wilmer W. Nichols, now at the University of Florida in Gainesville. My students and postdoctoral fellows have also contributed in a very real sense; I am grateful to them for their stimulating ideas and for joining me in the satisfying work of scientific enquiry. My sincere thanks go to Mr. Freddie Jackson, for his skillful assistance in the laboratory. My research work has been aided by grants from the National Institutes of Health, the National Science Foundation, and the American Heart Association.

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Contents

1

Introduction

Hemodynamics is a branch of hydraulics, and to the extent that it exists as a separate discipline, it owes its identity to the peculiar properties of blood and the vascular tree, which do not behave in accordance with the simplest forms of the relevant physical laws. Fluid dynamics, in its broadest sense, comprehends all of these peculiarities, but blood flow in living animals is far from the idealized motion of simple fluids through smooth cylindrical tubes, and the myocardium and blood vessels are not the homogeneous materials of engineering textbooks. There is consequently a body of literature concerned specifically with what might be called the biophysics of the circulation, in which such topics as the anomalous viscosity of blood and the viscoelasticity of blood vessel walls find a natural place. Physicists and mathematicians, physicians, and physiologists have all contributed to this literature, and reports that relate to hemodynamics are scattered through a great variety of journals and monographs. One of the goals of a volume like the present one is to synthesize material from such diverse sources.

Three different lines of interest converge in hemodynamics: the physical properties of the heart and blood vessels, the relation of these properties to the phenomena that are observed in the circulation, and the application of the results to physiological research or clinical medicine. All three involve the physiological as well as the physical characteristics of the circulation, for the laws that govern the flow of blood, unlike those that apply to oils or paints, operate in structures whose properties are imperfectly known. An understanding of hemodynamics is scarcely possible without some knowledge of cardiovascular physiology, and particularly of the inherent properties of cardiac and vascular tissues. The activities of these tissues conform to the general laws of Nature—the doctrine of vitalism is long dead— but their performance could not be predicted *a priori* without more knowledge than we now possess. The force generated by a piece of cardiac muscle is proportional to its initial length, but that fact is known only by virtue of repeated experiments, and it is difficult to see how it could have been predicted in advance.

Basic physiological information of this kind, essentially empiric in nature, is thus a prerequisite to discovering the physical relationships with which hemodynamics is concerned. The dynamic laws that apply to the motion of the blood are but one aspect of cardiovascular function, a set of principles that help us to understand certain events, and a set of tools for extracting information from experimental observations. Cardiovascular physiology includes a vast range of other topics, but physiological responses *per se* will be discussed here only when they are essential to understanding the experimental approach to a problem or when they throw light on dynamic conditions. It will be assumed that the reader has had at least an introduction to mammalian physiology, which is provided by many modern textbooks.

Pulsatile phenomena are emphasized in this work for a good reason. Until recently, the most familiar principles applied to the study of cardiovascular physiology were those of what might be called *steady-flow hemodynamics*. The motion of the blood is first and foremost a pulsatile phenomenon; yet the study of oscillating waves in the circulation was long confined to a few research laboratories. In most physiological experiments, circulatory function was not expressed by measurements of the pulsations generated by the heart, varying with time throughout the cardiac cycle, but instead by mean flow and pressure, averaged over a number of heartbeats. Cardiac output was commonly measured, but it is an average of ventricular outflow over a period of seconds or minutes. The reason for this concentration on average values was the difficulty in measuring instantaneous flow *in vivo* and the complex calculations required to analyze the results. The development of electromagnetic and ultrasonic flowmeters overcame the first of these obstacles, and the increasing availability of digital computers disposed of the second. This is not to say that average pressures and flows are of no value, but only that pulsatile blood flow can be regarded as a steady, or average, motion on which pulsations are superimposed and that both components are important. Techniques for recording pulsatile pressures preceded those for pulsatile flow by some years, but the ability to measure both simultaneously gives much more information about the properties of the system.

Steady-flow hemodynamics is the foundation for the more complex considerations involved in pulsatile flow and is consequently presented first in Chapter 2. The derivation of Poiseuille's law as an idealized relationship leads to the concept of vascular resistance, the consideration of the hydraulic energies associated with blood flow, and the consequences of nonlaminar flow. Further development requires an understanding of the rheological properties of blood and the vessel wall, which are treated accordingly in Chapters 3 and 4. This establishes a basis for the analysis of pulsatile flow in Chapter 5, where Womersley's (1957a) equations are used to introduce other linear and nonlinear models as well as the relevant experimental observations of blood pressure, flow, and velocity profiles.

Models, usually in the form of mathematical expressions, play an important role in hemodynamics. In essence, they embody the assumptions that we make about conditions in the circulation and state them explicitly and quantitatively so that they can be tested by experiment. It must be added that the sections on steady and pulsatile pressure-flow relationships are concerned primarily with blood vessels greater than 200 μm in diameter. The microcirculation is a special case (p. 150), and hemodynamic conditions in the arterioles, capillaries, and venules are still not fully understood (Charm and Kurland, 1974; Cokelet *et al.,* 1980), although newer techniques for measuring pressure and flow in microvessels (p. 307) have greatly stimulated research in this field.

To furnish a quantitative background for the physical properties that have been discussed, a survey of the normal range of the most important hemodynamic variables in mammals follows in Chapter 6. Specific ideas and phenomena that have only been mentioned up to that point are then treated in detail: the physical properties embodied in the concept of vascular impedance, the consequences of wave reflection, and the analysis of travelling waves (Chs. 7–9). Turning from the blood vessels to the heart in Chapter 10, the mechanics of ventricular function are considered. The last two chapters deal with the experimental measurement and analysis of data. Certain technical details are contained in four appendices at the end of the book, followed by a list of physical units, conversion factors, and symbols used in the text.

In keeping with the intention of providing a work of reference, most topics have been treated in considerable detail, including derivation of the most important equations. Readers who are approaching the subject for the first time should not hesitate to skip these derivations and aim for a broad understanding of general principles and their consequences. The development of Womersley's equations can well be postponed on an initial reading, for example. Throughout the work, I have attempted to show the interplay between theory and experiment, two aspects of hemodynamics that sometimes advance at different rates but must be brought into congruence from time to time. In treating most subjects, I have used an historical approach, believing that the successive steps in the development of hemodynamics provide the key to understanding its present state. For that reason, an extensive list of original papers is included, and appropriate references are cited throughout the text.

Indispensable as such original reports are, they should be thought of as part of an historical sequence. Progress in this field has been erratic, a succession of fallow periods alternating with sudden spurts of insight. The history of the subject sets these events in perspective, showing in retrospect how one advance led to the next, and perhaps pointing to the paths that lie ahead. Many excellent works have been devoted to this topic (*e.g.,* Franklin, 1933; Mettler and Mettler, 1947; Leake, 1956; Fishman and Richards, 1964; Fulton and Wilson, 1966). The following account is no more than an outline of the main points relevant to hemodynamics.

THE HISTORICAL DEVELOPMENT OF HEMODYNAMICS

William Harvey's unequivocal description of the circulation of the blood is rightly considered the first step on the path to modern cardiovascular physiology. His discovery did not arise *de novo*, however, for the working of the heart and blood vessels had been an object of serious enquiry for centuries before he published his classic work in 1628. The fact that the heart alternately contracts and relaxes under its own power was known in the pre-Christian era, and Harvey himself acknowledged his debt to Aristotle. The probable existence of some kind of communication between arteries and veins was recognized by the Greek scientist Erasistratus in the 3rd century B.C., although Erasistratus shared with his predecessors the notion that the arteries contained air rather than blood. This misconception probably goes back to Aristotle's use of strangulation as a method of slaughtering animals before study, as T. H. Huxley (1880) first pointed out. The veins and right side of the heart are engorged with blood under such conditions, whereas the left heart and arteries are relatively small. Since the arteries do not collapse, they appear hollow and admit air when cut across in dissection (Fulton and Wilson, 1966).

Medieval students of the circulation were largely concerned with its structure, a field that attained the status of an art in the collaboration of the anatomist Andreas Vesalius (1514–1564) and the artist Jan Van Kalcar, a student of Titian. Such studies of cardiovascular anatomy were an essential preliminary to later studies of function, but curiosity about the way the structures worked was by no means lacking. Leonardo da Vinci (1452–1519), for example, mentioned in his writings that the contraction of the heart lasted about half as long as the resting period and built glass models of the heart valves to illustrate their function. The first book devoted solely to bodily functions was written in da Vinci's lifetime by Jean Fernel, who also originated the disciplinary name, "physiology" (Leake, 1956). Moreover, in the 16th century, Vesalius' assistant, Realdus Columbus, and Michael Servetus both described the passage of blood from the right side of the heart to the left through the lungs, rejecting the notion of Galen (130 to ca. 200) that it moved through pores in the ventricular septum.

The overwhelming significance of Harvey's work lay in the clear, scientific demonstration that Galen's description of an ebb and flow of blood in the arteries could not be correct. The weight of Galen's authority had sustained this belief for generations, and continued for some years to foster disbelief in the new assertion that blood moved in a circle. Harvey's contribution to the gradual replacement of authority by experiment was only one, but not the least, of his achievements. His skill in conceiving simple experiments is evident in his demonstration of the direction of venous flow, controlled by valves, in the forearm, an experiment illustrated by classic engravings that still appear in many textbooks of physiology.

Quantitative reasoning, the hallmark of modern science, was an essential part of his method, for he estimated the stroke volume of the ventricles by measuring their capacity and showed that the heart must pump out in a few minutes a volume of blood greater than that contained in the whole body. The implication that blood returns to the heart by another pathway was only one of a host of arguments and observations that he assembled. The measure of his work, as of all fundamental discoveries, is that it changed thinking to such an extent that we can now scarcely understand how anyone could have thought otherwise. The invention of the compound microscope in the next generation enabled Malpighi to see the systemic capillaries, demonstrating morphologically the arteriovenous communications that Harvey could only postulate.

Harvey can thus be regarded as the founder of hemodynamics, among other things, beginning the application of physical principles to the study of the cardiovascular system. The development of hemodynamics after Harvey was part of the great surge of scientific activity in the 18th and 19th centuries, which led mathematicians and physicists as well as physiologists and physicians to examine the motion of blood and the forces involved in it, applying to the circulation the same laws that were being discovered for inanimate systems. The foundation of modern hemodynamics was laid by Isaac Newton's work on the property of fluids called viscosity, and by his concepts of force, mass, and acceleration.

The greater part of hemodynamic theory today stems from Newton's laws, which are cited in every physics textbook, and from Galileo's studies of mechanics.

Methods of Measurement

As is frequently the case, advances in knowledge paralleled the development of new methods of measurement. Stephen Hales, the curate in a village outside London, deserves a place beside Harvey as one of the founders of physiological measurements of cardiovascular function. He measured blood pressure by inserting a tube in the artery of a horse and noting the height to which the blood rose, measured ventricular volumes in several species by making wax casts, and expressed the concept of peripheral resistance. In 1733, he published these studies in a volume called *Haemastatics*, describing his experiments with a clarity and precision that would meet the standards of any modern scientific journal. The major impact of Hales' work was not the exact values that he obtained (although many of his results are not far from modern estimates), but the example set by devising appropriate experiments and applying simple mathematics in their interpretation.

Curiously enough, although this demonstration engaged the interest of Hales' fellow members of the Royal Society, no further advances in the measurement of blood pressure appeared for another hundred years, when Carl Ludwig introduced graphic recordings in 1847. Ludwig's institute at Leipzig was a world center of physiology in the 19th century, and the invention he called a *kymograph* was but one of his many contributions to science. The inscription of records on a moving surface may seem a minor technical achievement, but it ensured that variations with time in the cardiac cycle were recognized as an important variable, and such records later became a common feature of physiological experiments. The history of graphic recording has been recounted by Hoff and Geddes (1960). Many investigators became interested in the technical problems of manometry in subsequent years, and a succession of pressure-measuring instruments appeared (see Ch. 11)—fluid-filled tambours covered by a rubber membrane and connected to an intravascular sound (Marey, 1881), mirrors cemented to the membrane to produce records by photographic means (Wiggers, 1928), and eventually the introduction of electrical transducers.

The measurement of blood flow, or at least the cardiac output, can be said to have started with Harvey's estimation of ventricular stroke volume from the capacity of the chamber post mortem, but physiological observations of cardiac output did not begin until the late 19th century. Adolf Fick, a German physiologist who was equally accomplished in mathematics and physics, was the first to devise an appropriate method, in 1870. The velocity of blood flow had been estimated in 1829 by Hering, who measured the transit time of an injected substance from one point in the circulation to another, but Fick devised the first procedure for determining the ventricular output in liters of blood per unit time. What is now called the *Fick principle* is a simple yet penetrating insight into the relation between blood flow and the transport of respiratory gases. If one measures the concentration of oxygen in the blood entering and leaving the lungs, he reasoned, and also the volume of oxygen taken up in the lungs per minute, then the volume of blood that passed through the lungs in that time can be calculated (see Ch. 11). The same principle applies to carbon dioxide transport, or for that matter to foreign gases, and the flow of blood through the kidney and other organs can be measured in a similar way. Zuntz and Hagemann used the method in 1898 to measure cardiac output in the horse. Krogh and Lindhard devised a similar method in 1920, based on the inhalation of a foreign gas that is taken up in proportion to the pulmonary blood flow. A modification of this technique was adopted by Grollman, who published an extensive series of results on human subjects in 1932, although his estimations are now known to be falsely low.

The standard Fick method is highly reliable, but its application is limited by the requirement that the oxygen content of the blood entering the lungs through the pulmonary artery must be measured. Samples of blood from peripheral veins will not serve the purpose, because the oxygenation of blood returning from different parts of the body varies and the blood is further modified in the right atrium by inflow from the coronary sinus. For a long time, this fact restricted the method to experimental animals, where blood could be withdrawn from the right ventricle or the pulmonary artery itself. With the advent of cardiac catheterization in human subjects, a procedure that was introduced by Forssmann in 1929 and first used extensively by Cournand and Richards in 1941 (see also Cournand and Ranges, 1941), it became possible to use the Fick method in man, with enormous benefit to clinical investigation and practice.

A second method of determining cardiac output, the indicator-dilution technique, appeared about the turn of the century, when Stewart used the dilution of injected salt solution to measure circulation time and blood flow. After Stewart's publication in 1897, Henriques modified the procedure by injecting a single bolus of indicator (thiocyanate) and measuring the resulting rise and fall of indicator concentration downstream (1913). The injected material must be thoroughly mixed with the bloodstream before reaching the distal sampling site; modern versions of the method generally use an injection into the systemic veins or right heart and record the resulting concentration curve after passage through the heart and lungs into the systemic arteries. The technique was largely refined to its present state by the work of Hamilton and his associates between 1927 and 1948. Indicator-dilution methods are now the most widely used procedures for measuring cardiac output experimentally or clinically, and the principle has been extended to thermal or radioisotope dilution.

The measurement of pulsatile blood flow, recording the velocity in a blood vessel at every instant, has a shorter history. Priority in this regard apparently belongs to Chauveau and associates, who described what is now known as a "bristle flowmeter" in 1860. This instrument, also used by Marey (1881), is based on the motion imparted by blood flow to a pendulum suspended (very stiffly) in the bloodstream. Later, investigators strove to reduce the inertia of the device; improved versions are still in use (see Cappelen, 1968). The bristle flowmeter and related instruments measure the force imparted by the bloodstream to a detector rather than the actual velocity of the blood.

A quite different approach to pulsatile flow is based on the measurement of pulsatile pressures and the assumption of some theoretic pressure-flow relationship. This method originated in Germany with Otto Frank (1899) and his followers, who developed it to determine stroke volume from records of aortic pressure (Frank, 1899–1930). The calculation of blood flow as a function of time from the recorded pressure gradient has been a goal of many investigators since then, and several different methods are in use today (Fry *et al.*, 1956; Fry, 1959; McDonald, 1974). It is necessary to make some assumptions about the physical properties of the arteries, but under the right conditions the results are a fair approximation of the true flow.

A number of other phasic flowmeters fall in the same category but infer the rate of flow from artificially induced pressure gradients. Most of these are based on a principle enunciated by the physicist Bernoulli, namely, that kinetic energy is converted into pressure, or vice versa, when the velocity of flow in a confined channel is altered (p. 21). An example is the *Pitot tube*, which detects the difference between *lateral* and *end* pressure in a vessel (see p. 23) and was used by Cybulski to measure blood flow in 1885. The *orifice meter* belongs to the same class but depends on the pressure difference across a constriction or pierced plate in the vessel lumen; it was used extensively to measure flow in the coronary and other arteries in the years from 1920 to 1955. A third method of flow measurement relies on direct observation of the motion of blood. Perhaps the most effective exploitation of this technique was carried out by McDonald (1952), who tracked the velocity of air bubbles in various arteries by means of high-speed photography. The lineal descendent of such procedures today is the metering of red-cell velocities by a television technique (p. 317).

All of these methods became obsolete when the electromagnetic flowmeter was invented, although some time elapsed before reliable models became generally available. These instruments make use of a fundamental electromagnetic principle discovered by Faraday in the 19th century, the generation of an electromotive force when a conductor moves through a magnetic field. Faraday himself was aware of the possibility of measuring fluid flow by this means and attempted in 1832 to measure the velocity of the river Thames as it moved through the magnetic field of the Earth. The instruments available to him and the small size of the signals defeated this effort, and the same problems were encountered by later scientists who attempted to measure blood flow in the same way. Given the relatively low velocity of the bloodstream and the limited size of the magnets that could be incorporated into a perivascular cuff, the flow signals required great amplification, and the first blood flowmeter to operate on the electromagnetic principle was not constructed until 1932, by Fabre. A practical instrument was developed independently in 1936 by Kolin, who is largely responsible for the subsequent development of the relatively trouble-free electromagnetic flowmeters now in use. Wetterer (1937) and Wyatt (1961) are also prominent among those who have brought the method to its present state.

The ultrasonic flowmeter, introduced by Rushmer and his colleagues at the University of Washington in 1961, has now taken its place beside the electromagnetic type (Franklin *et al.*, 1961). Ultrasonic methods entered physiology as an aftermath of the second World War, where "sonar" played an important role in the detection of underwater craft. The wave of technological advances that began after that conflict included the improvements in electronics that led to accurate and sensitive manometers, oscillographic recorders, and the electromagnetic flowmeter, as well as the use of ultrasound to measure cardiac dimensions and blood flow. *Echocardiography*, an external method of measuring ventricular dimensions and motion by means of ultrasonic transducers on the chest wall, has become a common diagnostic procedure in clinical medicine. Two methods of measuring blood flow were developed, one based on the Doppler phenomenon, the other on the transit time of ultrasonic waves in the bloodstream. Various kinds of "noise" were a serious problem in the early instruments, but these defects have been overcome to a large extent. Noninvasive ultrasonic probes that can measure flow contours in superficial arteries through the intact skin have opened up a whole new research field.

Theories of Hemodynamics

To trace the beginnings of hemodynamic theory, we must return again to the 18th century, where two distinct ways of thinking about the circulation had their origin. One was rooted in Hales' emphasis on arterial elasticity as the means by which the intermittent ejection of blood by the ventricles is transformed into a much less pulsatile flow in the periphery. The other was directed at the manner in which pressure and flow waves change as blood moves through the circulation. Like others before him, Hales observed that arterial flow persisted after each contraction of the ventricles, and concluded that this late flow came about because of the elastic recoil of the vessels. Unlike his predecessors, he elevated this observation into a theory by a metaphor so vivid that it has influenced hemodynamics ever since. He compared the arteries to a mechanical device familiar to his readers:

> The blood is carried on in the finer capillaries, with an almost even tenor of velocity, in the same manner as the spouting water of some fire-engines is contrived to flow with a more even velocity, notwithstanding the alternate systoles and diastoles of the rising and falling embolus or force; and this by means of a large inverted globe, wherein the compressed air alternately dilating or contracting, in conformity to the workings to and fro of the embolus, and thereby impelling the water more equably than the embolus alone would do, pushes it out in a more nearly equal spout (Hales, 1733, p. 23).

The compression chamber of this analogy became "Windkessel" in the German translation, and the *Windkessel theory* is invoked to explain various circulatory phenomena to this day. The simile is well chosen; the volume ejected during each systole distends the proximal portion of the aorta and its branches, and the elastic energy thus stored in the walls of these vessels is reconverted to energy of flow as the walls recoil during diastole. The gradual decline of arterial pressure during diastole, contrasting with the abrupt drop that would be found in a rigid system of tubes, is a manifestation of this "buffering" action. Hales' comment was intended as a simple analogy, and it was not until 1899 that his description found a proponent, Otto Frank, who would give it the status of a quantitative model.

The work of Frank and his students, recorded in a series of papers extending from 1899 to 1930, gave great impetus to the study of hemodynamics. Many of his experiments were concerned purely with physiology, but his interpretations were always couched in terms of physical models or equations. The regulation of cardiac output, the work of the heart, the elasticity of blood vessels—all received his attention. Although he was well aware of the limitations of the Windkessel model, his work nevertheless did much to popularize it.

The principal flaw in the model is the absence of anything that represents the longitudinal motion of blood through the vascular tree. The aorta and major branches are treated as a single chamber, drained by a linear resistance. To the extent that wave velocity is thought of at all in such a model, it must be assumed to be infinite. For some purposes this concept served well enough, but as more sophisticated physiological questions were posed, the absence of transmission properties became a fatal defect. Frank (1905) pointed out that the velocity of pressure waves in the circulation is finite, and he modified the Windkessel to include traveling waves and reflections.

Later, followers in Germany (Wezler and Boger, 1939; Wetterer, 1940) and in America (Remington and Hamilton, 1945, 1947) set out to determine the "length and breadth" of the hypothetical distensible chamber, producing meticulous measurements of the dimensions of the aorta and large arteries in the dog and man. Multichamber models and nonlinear elastic properties were proposed (for references see p. 102), but, as Aperia (1940) pointed out, these added refinements did nothing to overcome the fundamental inconsistency in a hypothesis that postulated infinite wave velocities for some purposes and finite velocities for others. In recent times, the motive for creating a satisfactory model of the Windkessel type has been to use the corresponding equations to calculate stroke volume from measurements of aortic pressure, which are relatively easy to record in a hospital environment. Several such models have been described, and often used successfully, but they have a disturbing tendency to fail in just those radically abnormal situations where the information is crucial.

An alternative way of thinking about pressure and flow in the circulation claimed the interest of prominent scientists long before Frank's analysis of the Windkessel, one that concentrated on the dynamic changes as blood progressed along a vessel. Those who took this view were not interested in representing the arterial tree as a single chamber, but rather in the changes in vascular properties along the length of vessels; it is perhaps correct to identify Daniel Bernoulli as the founder of this school of thought. Bernoulli (1700–1782), a Swiss physicist and mathematician, applied the relatively new laws of mechanical energy to hydraulic problems, simplifying the analysis by assuming a fluid that has no viscosity. (Such a liquid, rather presumptuously referred to as an "ideal" fluid, found many applications in the hands of later theoreticians.) The theorem for which he is now best known in circulatory physiology, called Bernoulli's principle, describes the conversion of kinetic energy into pressure when fluid moving in an enclosed conduit reaches a point where the cross-sectional area of the channel increases abruptly (see p. 20).

The experimental work of the French physician J. L. M. Poiseuille (1799–1869), which was published in detail in 1846, belongs to this same tradition in the sense that it dealt with changes in pressure along the length of a vessel. Poiseuille merits a prominent place in the history of hemodynamics because of the broad implications of his results, not to mention his invention of the mercury manometer in 1828. His formulation of the law that governs the steady, laminar flow of a viscous liquid through rigid conduits was based on purely empiric observations of the flow of water through glass tubes, but his results were very accurate (see p. 12). The theoretic equations of motion for viscous fluids had already been published but formed no part of Poiseuille's approach, which was entirely experimental. Navier published an analysis of such motion in 1822, and it was extended and corrected by Stokes in 1845 (Lamb, 1879). Poiseuille's results were in effect an experimental demonstration of the Navier-Stokes equations (see p. 104) in the special case of steady flow through rigid tubes, and the empiric constant in Poiseuille's original equation was in fact the term representing the viscosity of the fluid.

An equally important thread of this story concerns the velocity with which pressure waves are transmitted through blood vessels, which is quite different from the speed with which the blood itself moves. The development of theories about this phenomenon can be traced back to Euler in 1755. Euler postulated that the ventricular ejection of blood created a wave that was transmitted through the arteries with a finite velocity, and attempted without success to formulate appropriate equations. The problem involves much more than the viscous damping in fluids, because the distensibility of the vessel and the motion of its walls must be taken into account. Not until 1850 was a satisfactory solution announced by the Webers, three remarkable brothers who made a variety of contributions to physiological knowledge. Wilhelm Weber had developed theoretic equations for the wave velocity in an elastic tube, and his brother Ernst had made experimental measurements that were very close to the predicted values. They did not publish the full derivation of the equations until 1866, and it was then discovered that Thomas Young had reported a similar theoretic analysis some 50 years earlier. Young was a physicist of unusual range, whose most important work was in optics and color vision, although his name is attached to a standard modulus of elasticity. His equations on wave velocity probably went unnoticed because of their unconventional form and notation (Noordergraaf, 1969). Resal, in 1876, perceived that motion of the wall could be derived from pressure-radius relationships and introduced simple elastic theory into his own expressions for wave velocity, which he arrived at independently. The interest of these investigators was focused only on the *speed* of wave propagation; the simultaneous damping of wave amplitude by viscous attenuation did not receive serious attention until much later.

In 1878, Moens reported a careful series of experiments, and Korteweg a detailed theoretic analysis of wave velocity in elastic tubes, resulting in what is now known as the Moens-Korteweg equation (p. 97). Like almost all their predecessors, they simplified the problem by assuming a nonviscous fluid, which may account for Moens' observation that the theoretic equation had to be multiplied by an empiric coefficient to match the velocities he measured. Korteweg considered the effects of such complicating factors as longitudinal strain, wall mass, and fluid compressibility, although these variables were omitted from his basic equation. Lamb, who published a definitive work on hydrodynamics in 1879, probed these aspects of the problem more deeply and produced complete equations of wall motion, framed in terms of the elastic modulus of the wall. The first complete analysis of wave propagation that could be adapted to physiological studies was done by Witzig in 1914 and included the effects of fluid viscosity. His work appeared as a Ph.D. thesis for the University of Bern and was not widely circulated, with the result that years passed before similar analyses were arrived at independently by Morgan and Kiely (1954) and Womersley (1955a). All of these theorists adopted Lamb's formulation of the relations between pressure and radial motion of the vessel wall.

Womersley's work had a profound influence on much of the subsequent research in hemodynamics. The long series of papers that resulted from collaboration between Womersley and McDonald between 1955 and 1958, in particular, are indispensable reading for the modern student of the subject. Womersley's theoretic approach rested on a linear simplification of the Navier-Stokes equations, and his formulae were readily applied to experimental measurements of pressure, flow, and wall motion. Systematically, he contrasted the conditions in rigid, elastic, and viscoelastic tubes and finally the case of a tube constrained by external tethering and mass, a fair analogue of the artery *in vivo*. Fortunately, the Fourier analysis of pressure and flow waves that was an essential part of his approach had been suggested much earlier by Frank (1926), championed by Aperia (1940), and finally introduced into cardiovascular physiology by Porjé (1946). The close connection between theoretic analyses and experimental tests that Womersley and McDonald fostered led to many new concepts, including that of vascular impedance (Ch. 7); their students—Taylor and Bergel in particular—carried their work several steps further.

Womersley's mathematical models were derived from the equations of mechanics, but some other investigators sought to express the behavior of the circulation in terms of electrical circuits. The recognition that pulse waves are analogous in many ways to electrical currents travelling through transmission lines brought a large collection of engineering techniques to bear on the propagation of pressure and flow waves. The analogies are not perfect, but "transmission line models" of the vascular tree were found to be consistent with the phenomena observed in blood vessels and extremely useful in analysis (Landes, 1949; Taylor, 1959b). The existence of reflected waves was one of the many implications of such models and served to explain the otherwise puzzling increase of pulse pressure in the distal aorta.

A somewhat different usage of electrical analogy was adopted by others who actually constructed large electrical models of the entire circulation (Noordergraaf *et al.*, 1963). These analogues take advantage of the fact that resistors, capacitors, and inductances can be combined in arrangements that produce virtually any electrical impedance, and thus can simulate the vascular system. More often, electrical circuit diagrams were used simply as a source of appropriate equations and as a way of characterizing the circulation by a limited number of parameters. Mere simulation provides no new information, of course, and such modeling is of limited value unless the electrical components correspond to specific structures in the real vascular system, so that the values obtained have a clear physiological significance.

The interests of those who saw the circulation as a transmission system and those who saw it as a Windkessel were bound to converge as these lines of thought progressed, and many efforts were made to reconcile the two points of view. Otto Frank (1905) himself moved in this direction by modifying his first model to take account of damping and the mass of blood in the chamber. Efforts were later made to show that various models imitated the "natural frequency" and "standing waves" of the blood vessels (Remington and Hamilton, 1945, 1947), by analogy with the behavior of manometers, but these concepts were eventually shown to be invalid for the circulation, where attenuation and other factors prevent resonance (McDonald and Taylor, 1959). Many proposals were made to increase the number of chambers, the properties of their walls, and the connections between them, but the ultimate result of such revisions of the simple original concept is something very like the transmission line model. The great virtue of the initial Windkessel model was its simplicity, and it still has an explanatory value as a rough approximation that is readily grasped. For almost all research purposes, however, a more detailed and realistic model that conforms to the distribution of properties in the vascular tree is to be preferred.

In recent years, Guyton has introduced another way of thinking about circulatory dynamics in an effort to comprehend the circulation as a whole. His approach is not concerned with blood flow through individual vessels, but simplifies the problem by considering all of the systemic arteries as a single unit, characterized by a certain pressure gradient, volume, and flow, and treating the capillary and venous beds in the same way. The heart is also represented in Guyton's model, and indeed the crucial feature is the dependence of cardiac output on the filling pressure that appears at the end of the venous system. The model thus forces us to face the fundamental fact that the cardiovascular system is a circle.

The heart imparts energy to the blood and the vascular system determines the pressure gradients throughout the system in accordance with physical laws, but ventricular work itself is influenced physiologically by the pressure that remains to fill the right side of the heart (p. 273) at the end of the trip. The circulation is thus in a state of dynamic equilibrium, operating at a level that fits the existing conditions in both the heart and the vascular tree. Guyton and his associates (1957) made this point by calling attention to the resistance of the venous pathway from capillaries back to the right atrium and emphasizing that the "venous return" through these channels must equal the cardiac output except for very brief periods of readjustment. He described the relationships by sets of simple equations, showing how the contractile state of the myocardium, the total blood volume, the regional vascular compliances, and resistances all fit into a consistent steady state.

Like other fundamentally simple concepts, this one can be pushed beyond its limits, and some investigators have read cause and effect into mathematical expressions that merely state relationships. To say that the rate of venous return "controls" cardiac output, or that cardiac output "controls" venous return, is no more than tautology. A more useful way of stating the facts is that the properties of the heart and those of the blood vessels interact to determine hemodynamic conditions within the system. Extensive analogue models of the whole circulation have been based on this approach (Noordergraaf, 1969; Beneken, 1963), using expressions like those of Womersley to define pressure gradients and pulsatile transmission through the vessels.

As for the detailed mathematical models of the blood vessel, the Womersley equations were not the first, nor were they the last. Many investigators have devised others, some differing greatly and others only slightly from Womersley's version. At least 20 such models can be found in the literature (Cox, 1969), contrasting the effects of thin versus thick wall, constrained versus freely moving vessels, and linear versus nonlinear equations (see Table 5.3). The omission of the nonlinear terms in the Navier-Stokes equations was an obvious weakness in Womersley's treatment, though it made possible a relatively straightforward solution. Numerous nonlinear models have now been proposed (p. 124), approximating more and more closely to the conditions in living blood vessels. In recent years, the general availability of digital computers has encouraged such efforts by allowing scientists to formulate hypotheses with little constraint on the quantity of data or the intricacy of the calculations involved.

Nevertheless, hemodynamics is still vulnerable to Hinshelwood's criticism of 19th century fluid dynamicists, who were divided, he said, into ". . . hydraulic engineers who observed what could not be explained, and mathematicians who explained things that could not be observed" (cited by McDonald, 1974). The division is not now so sharp, and much more can be observed, but theories of flow in blood vessels have proliferated beyond our ability to test them experimentally. The gap is narrowing, but it is not likely that we shall be able in the near future to discriminate between hypotheses that differ by only 5% in their predictions. Such small differences may be critical in some special cases, but for the most part they are of little consequence and it would be best to get on with the physiological questions that can be answered with the help of the best available theory.

A much greater gap exists between the hemodynamic measurements that can now be made and our ability to interpret their significance. Progress along these lines is certainly to be expected; the evaluation of arterial viscoelasticity may well be an indirect clue to the behavior of vascular smooth muscle, for example, and may prove to be useful in clinical medicine as well as research. Conventional steady-flow dynamics, in the form of pressure and cardiac output measurements, has long been a standard part of cardiology, but the newly acquired knowledge of hemodynamics is slow to find its way into the cardiac catheterization laboratory. History teaches that this is normal, and only temporary. Today's esoteric fact has a way of becoming tomorrow's routine diagnostic test.