CHAPTER 1

PHYSIOLOGICAL INTRODUCTION

The overall arrangement of the mammalian cardiovascular system can be summarised briefly as follows. The heart is composed of four chambers arranged in two pairs. The thin-walled atrium on each side is connected through a valved orifice to a thick-walled muscular ventricle; each ventricle connects in turn to a major distributing artery, the mouth of which is again guarded by a valve. The left ventricle is the thicker and leads to the aorta (diameter about 2.5 cm in man), through which oxygenated blood is distributed to the tissues of the body. Large arteries branch off the aorta, smaller ones branch off them, and so on for many subdivisions; the number of branchings along any pathway depends on the particular organ being supplied. The final subdivisions of the arterial tree are the arterioles, which have very muscular walls and internal diameters in the range 30–100 μm. These vessels give rise to the capillaries (diameters down to 4 or 5 μm) across the walls of which the principal exchange of fluids and metabolites between blood and the tissues takes place. The blood passes from the capillaries into the smallest veins (venules) and thence into a converging system of increasingly larger veins, finally merging into the superior and inferior venae cavae which join directly to the right atrium of the heart. (An exception to this pattern is the circulation in the heart muscle itself, which drains directly into the right atrium.) From the right atrium, blood is transferred to the right ventricle, and thence to the pulmonary artery, which leads through a bifurcating system of arteries to the pulmonary capillaries in the walls of the alveoli of the lung, where gas exchange takes place. From there the re-oxygenated blood is returned to the left atrium via the pulmonary veins, and the cycle is repeated. The average time taken for an element of blood to complete one circuit of the system is about one minute (in man).

The aim of this book is to explain the physical processes involved in the circulation of the blood in the large vessels of the circulation. The microcirculation (arterioles, capillaries and venules) is excluded for the reasons given in the preface; it is convenient that the conventional definition of the microcirculation, as consisting of all vessels which cannot be seen except through a microscope (i.e. of diameter less than about 100 μm), conforms closely to a definition more appropriate from the fluid mechanical point of view, namely vessels in which the mean Reynolds number is normally less than 1. Thus we shall be concerned with aspects of the circulation for which fluid inertia is important, and, as it turns out, for which blood can be considered a homogeneous Newtonian fluid (see § 1.2). This chapter is intended to set the scene by describing both the physical properties of the system and the phenomena which it is physiologically important to analyse. We also consider the fluid mechanics of the left ventricle in § 1.3.

Many books and reviews have already been published on the fluid mechanics of the circulation. Among the most important, on which I have leaned heavily for the material of this chapter and the next, are the two editions of *Blood Flow in Arteries* by McDonald (1960, 1974), the two-volume work edited by Bergel (1972*a*), Bergel & Schultz (1971), chapters 12 and 13 of Lighthill (1975) and the proceedings of various symposia (Attinger, 1964; ASME, 1966; Fung, 1966; Fung, Perrone & Anliker, 1972). Considerable detail on the structure and properties of the whole cardiovascular system, together with much physical (but not mathematical) discussion of the fluid mechanics, is given in a book of which I am a joint author (Caro *et al.*, 1978); most of the information in § 1.1 of this monograph is also contained in that work.

1.1 Anatomy, wall structure and mechanical properties

While the principal aim of the study of cardiovascular mechanics is to understand the circulation in man, most experimental data have been obtained in other mammals, especially dogs. Where the difference is important in what follows, it is mentioned; usually, however, the fluid mechanics is not well enough understood for

small inter-species differences to be important except in the matter of scale. Most of the quantitative values to be given will apply to the dog.

1.1.1 *The heart*

The two atria are comparable in structure, and are separated from each other by a common wall, the inter-atrial septum. The veins drain into them without valves. The atrio-ventricular valve on the right side has three cusps (or flaps) while that on the left (the mitral valve) has only two. In each case the edges of the cusps are tethered to the opposite wall of the ventricle by fine cords anchored in small slips of muscle (papillary muscle). These cords have no active function in the opening or closing of the valves, which occur passively (see § 1.3), except to prevent the valves turning inside out and allowing backflow when they have closed. The exit valves from the ventricles (the pulmonary and aortic valves) are similar to each other, each consisting of three cusps that can open to the full cross-section of the artery without coming into contact with the artery wall, because behind each cusp is an outpouching of the artery, or sinus. In the aorta these sinuses are called the sinuses of Valsalva; the coronary arteries branch off two of them. The sinuses have an important function in the operation of the valve, as discussed in § 1.3.

The four valve orifices in the heart are aligned approximately in the same plane (fig. 1.1), and the cusps of each are attached at their bases to a stiff ring of fibrous tissue. The four rings are in turn connected to each other by fibrous tissues, so that the valve plane forms a stiff framework to which the muscles of all the chambers are attached, as are the origins of the pulmonary artery and the aorta. The heart as a whole is slung in a thin but inelastic fibrous bag, the pericardium, which in turn is attached to other structures within the chest, including the spine. The stress–strain relation of the pericardium is, like all fibrous tissues consisting largely of collagen, highly non-linear. Under normal conditions the pericardium is relatively unstretched, and has little effect on pressures and volumes in the heart; in certain diseases, however, fluid accumulates in the pericardium, which becomes taut and constrains the maximum volume of the heart.

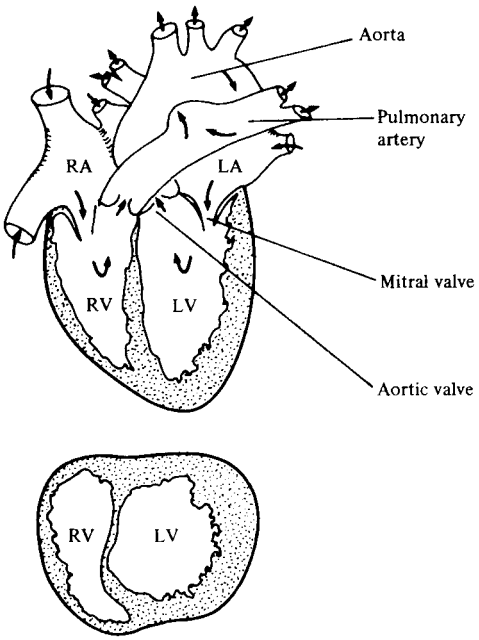

Fig. 1.1. Schematic diagram of a longitudinal and a horizontal cross-section of the heart, showing inflow and outflow tracts and valvular arrangement. Note the differences in the shape of the cross-sections and in the wall thicknesses of the two ventricles. RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium. (After Attinger, 1964.)

The left ventricle is shaped rather like a blunted arrowhead with the valves at its base (fig. 1.1), and with a roughly circular transverse cross-section. When the ventricle contracts, but before the aortic valve opens, the long axis first shortens slightly while the transverse cross-section expands so that the included volume remains constant. However, when ejection begins, the long axis shortens only very little, while the transverse axes shorten by about a third: by the end of systole (the ejection phase) the ratio of long to short axes is about 2.5 to 1, having been about 1.5 to 1 in diastole (the resting phase). A reasonable model of left ventricular shape, for the purposes of fluid mechanical calculations, is that of a prolate spheroid, whose major axis remains constant during ejection, but whose minor axes contract significantly. The two valves would both be at one end of the spheroid. This model involves considerable

approximation, but the inaccuracy of measurement of ventricular dimensions *in vivo* is so great that the approximation is not unjustified. The end-diastolic volume of the left ventricle in a 20-kg dog is about 40 cm^3, and about 20 cm^3 is ejected each beat (the corresponding figures in man are 140 cm^3 and 70 cm^3).

The right ventricle has been studied far less thoroughly than the left, but it is known to behave very differently. One wall is functionally part of the left ventricular wall, while the other, free wall is much thinner and has a larger area, so that the cavity of the right ventricle is wrapped round one side of the left ventricle like a pocket, opening at the top into the pulmonary artery and right atrium (fig. 1.1). The operation of the right ventricle is like that of a check-valve pump (Carlsson, 1969): during systole the free wall moves downwards, carrying the open pulmonary valve past the blood in the ventricle; during diastole it moves up again, the closed valve pushing the blood up with it. It is clear from continuity considerations that the amount of blood ejected each beat by the right ventricle must, on average, be the same as that ejected by the left.

The walls of the chambers of the heart consist almost entirely of muscle fibres, interspersed with collagen. Cardiac muscle is a form of striated muscle, as is skeletal muscle, but it differs in its electrical and mechanical properties. For instance, continuous stimulation of skeletal muscle held at a fixed length produces a sustained contraction (or tetanus) with a highly reproducible tension; this is the maximum tension that can be generated by that muscle at that length. Continuous stimulation of cardiac muscle, however, does not produce a tetanus, because the muscle repolarises slowly, so experiments to investigate its intrinsic contractile properties have to be much more elaborate (for example, a series of individual 'twitches' is commonly generated). Further, Hill (1938) showed experimentally that when tetanised skeletal muscle fibres contract against a constant force F, then (a) the rate of heat production is proportional to the speed of shortening V (i.e. equal to aV, say, where a is a constant), and (b) the total rate of energy production is linearly related to F, i.e.

$$(F+a)V = b(F_0 - F), \tag{1.1}$$

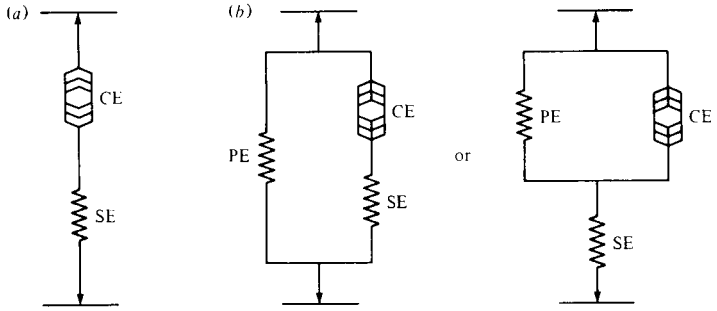

Fig. 1.2. Models of skeletal muscle. (a) A contractile element (CE) and an elastic element in series (SE); there is no tension when CE is relaxed. (b) Two possible arrangements in which a parallel elastic element (PE) supplies a 'resting tension'.

where b and F_0 are also constants. These results were obtained when the length of the muscle fibre at the start of the contraction was short enough for the 'resting tension' to be negligible, in which case a muscle fibre can be modelled as a 'contractile element' in series with a 'series elastic element' (fig. 1.2(a)). At greater lengths there is an initial tension in unstimulated muscle. This has to be accounted for by incorporating a 'parallel elastic element' into the model (fig. 1.2(b)), and by permitting a, b, F_0 in (1.1) to be functions of length, L.

No simple equation like (1.1) is applicable to heart muscle, however. This is partly because heart muscle cannot be tetanised, partly because individual muscle fibres cannot be separated as easily as in skeletal muscle, so the experiments are performed on small strips of (cat) papillary muscle in which some muscle fibres may not be parallel to the sides of the strip, and partly because at all lengths from which contraction is possible there is a significant resting tension. The absence of a tetanised state means that the time from the beginning of a twitch is an important variable in any relation between length, tension and velocity for cardiac muscle fibres, and no single model has been generally agreed. Fung (1970) has proposed the following equation, which can accommodate general non-linear and viscoelastic 'elastic elements':

$$\frac{\mathrm{d}\Delta}{\mathrm{d}t}(S, \Delta, t) = \frac{\pm b(\Delta)}{a(\Delta)+S}\left|\left[S_0(\Delta)\lambda \sin\frac{\pi(t+t_0)}{2t_m} - S\right]\right|^n. \quad (1.2)$$

In this equation Δ is the length of overlap between the actin and myosin filaments in the muscle sarcomere (a more fundamental measure of contractile element state than fibre length L), S is the stress in the series element, $S_0(\Delta)$ is the maximum attainable isometric tensile stress at overlap length Δ, n is an exponent whose value lies between 0 and 1 (in many cases being in the range 0.5–0.6), t_0 is a phase shift signifying the sudden initiation of active state at the time of stimulation, $2t_m$ is the time to peak activity, λ is an amplitude factor, $a(\Delta)$, $b(\Delta)$ are variable functions corresponding to a and b in (1.1), and the + or − is chosen according to whether the quantity in the square brackets in (1.2) is positive (stretching) or negative (relaxing). Equation (1.2) has the capacity to describe virtually all experimental results, but detailed testing of it, and empirical or theoretical evaluation of the functions and constants involved, are far from complete. Progress is necessarily piecemeal; for example, Brutsaert & Sonnenblick (1969) have shown that S_0 varies approximately linearly with length over a wide range of lengths:

$$S_0 = k_1 L + k_2, \tag{1.3}$$

where k_1 and k_2 are physiological constants.

A major practical difficulty with using (1.2) is the fact that most of the experiments on papillary muscle preparations have ignored two important factors: (*a*) the ends of the strips of muscle are inevitably damaged when clamped in the apparatus (Krueger & Pollack, 1975), and (*b*) even if they are not damaged, the strain in the middle section of a strip will differ from that at the constrained ends; this was demonstrated theoretically from finite-deformation elasticity theory by Hunter (1975). All the experiments therefore need to be repeated. Thorough reviews of the state of knowledge of heart muscle mechanics are given by Blinks & Jewell (1972) and by Caro *et al.* (1978, chapter 11).

Even if a model of the behaviour of heart muscle fibres were generally accepted, applying it to describe the mechanical behaviour of the intact heart would be extremely difficult. This is because of the intricate way in which the muscle fibres are arranged within the heart wall. The left ventricle is the only chamber whose

wall structure has been examined systematically. In it there is a continuous distribution of fibre orientation across the wall thickness. The innermost fibres run predominantly longitudinally from the stiff region round the valves (the base) to the other end of the chamber (the apex), which is an elongated cavity with roughly circular cross-section. The next layer of fibres is at a slight angle to the axis of the chamber, so that the fibres form a slight spiral. The angulation of the spiral increases in successively deeper layers, so that approximately half-way through the wall the fibres run circumferentially round the small cross-sections of the chamber. Thereafter the angulation continues, so that the outermost fibres are again longitudinal. Streeter *et al.* (1970), who described this arrangement, also used it as the basis for a prediction of normal and tangential stresses throughout the wall, on the assumption that each muscle fibre exerts the same tension. Predictions were made both for diastole, when the muscle is relaxed, and for systole, when it is contracted. In each case the tangential (hoop) stress is predicted to be greatest in the middle layers of the wall, with a slight bias to the outer surface in systole, while the normal stress is predicted to be greatest on the surface, especially on the inner surface during systole (when the pressure in the ventricle exceeds that outside by about 16 kN m^{-2}, or 120 mmHg). It would be possible to use an equation like (1.3) in Streeter *et al.*'s model, in order to incorporate more details of muscle behaviour, especially during contraction, but without more information on the resting lengths and tensions of the individual fibres, such predictions would be almost worthless. Without them, however, there is no link between the mechanics of individual muscles and that of the intact ventricle, and the latter must be described empirically.

Note that it is important to know something of the stress distribution in the ventricle wall, because the blood supply to the heart muscle is carried in coronary arteries which are embedded in it, and are therefore squeezed when the muscle contracts. Since coronary artery disease is one of the major causes of death in Western society, all information on coronary artery mechanics has potential clinical importance.

From the point of view of the rest of the circulation, contraction of the left ventricle produces a certain flow-rate into the aorta, Q_a,

and a pressure, p_a, at its entrance. Thus an index of the effectiveness of the ventricle can, in principle, be obtained by measuring these quantities. However, no satisfactory index of 'cardiac contractility' has yet been proposed, because the chain of events linking muscle performance to aortic pressure and flow-rate has not been fully described. In § 1.3 we analyse a small link in that chain by examining the relation between aortic pressure and flow-rate (relatively easy to measure *in vivo*) and the mean pressure exerted by the ventricular muscle, p_v, together with ventricular volume, V. The former can be related to the average tension in the ventricle wall, and hence to Streeter *et al.*'s model, as long as both V and the shape of the ventricle, as it contracts, are known. However, no accurate way of measuring V is available, and only qualitative observations of the shape have been made, as described above. Quantitative details of the time variation of ventricular and aortic pressures, and of aortic flow-rate, are given in § 1.2.

1.1.2 *The systemic arteries*

The anatomy of the canine aorta and its main branches is illustrated in fig. 1.3, and many of the relevant dimensions are listed in table 1.1 (which was first published in Caro, Pedley & Seed (1974)). The initial part of the aorta, after the sinuses of Valsalva, is relatively straight for about 3 cm and is called the ascending aorta. The aorta then curves, in a complicated three-dimensional way, through about 180° (the 'arch'), giving off two branches to the head and upper limbs (there are normally three branches in man). It then pursues a fairly straight course down through the diaphragm (giving off nine pairs of small intercostal arteries) to the abdomen, where it distributes branches to the abdominal organs. Low down in the abdomen it terminates, forming two iliac arteries and the sacral artery (absent in man). All other large arteries, similarly, are curved and branched in a complicated way; there are relatively few straight segments of artery without branches where the fluid mechanics of long straight tubes can be applied, and more general theories are usually required.

The aorta (like most other arteries) tapers along its length. The rate of taper appears to be quite variable from animal to animal and, presumably, from species to species; however, in the dog, the area

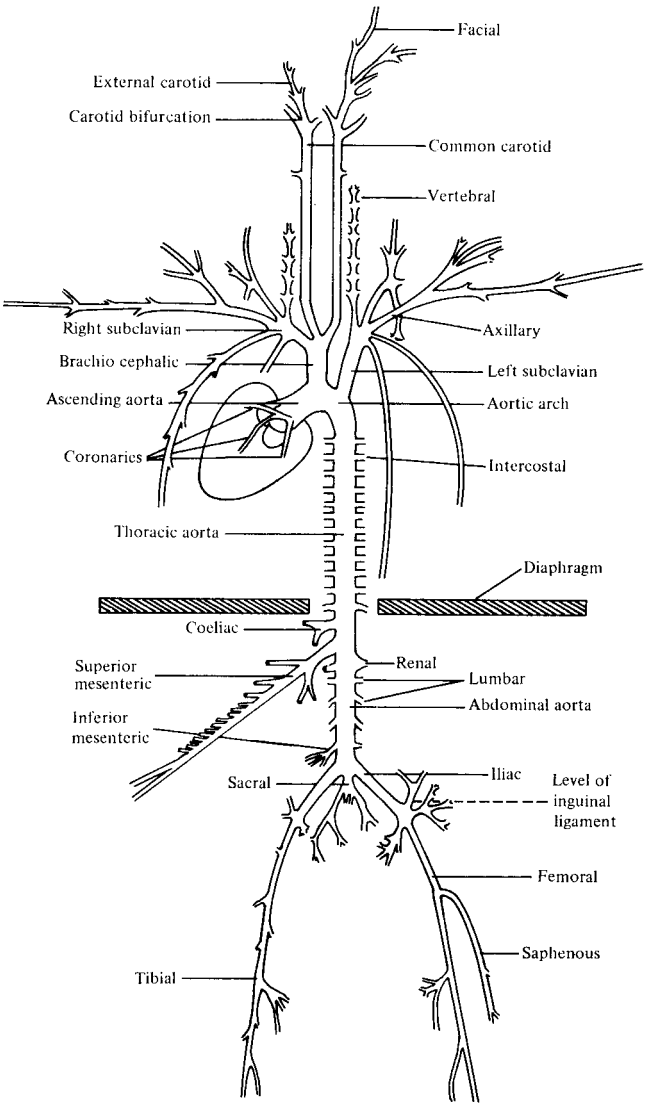

Fig. 1.3. A diagrammatic representation of the major branches of the canine arterial tree. (After McDonald, 1974.)