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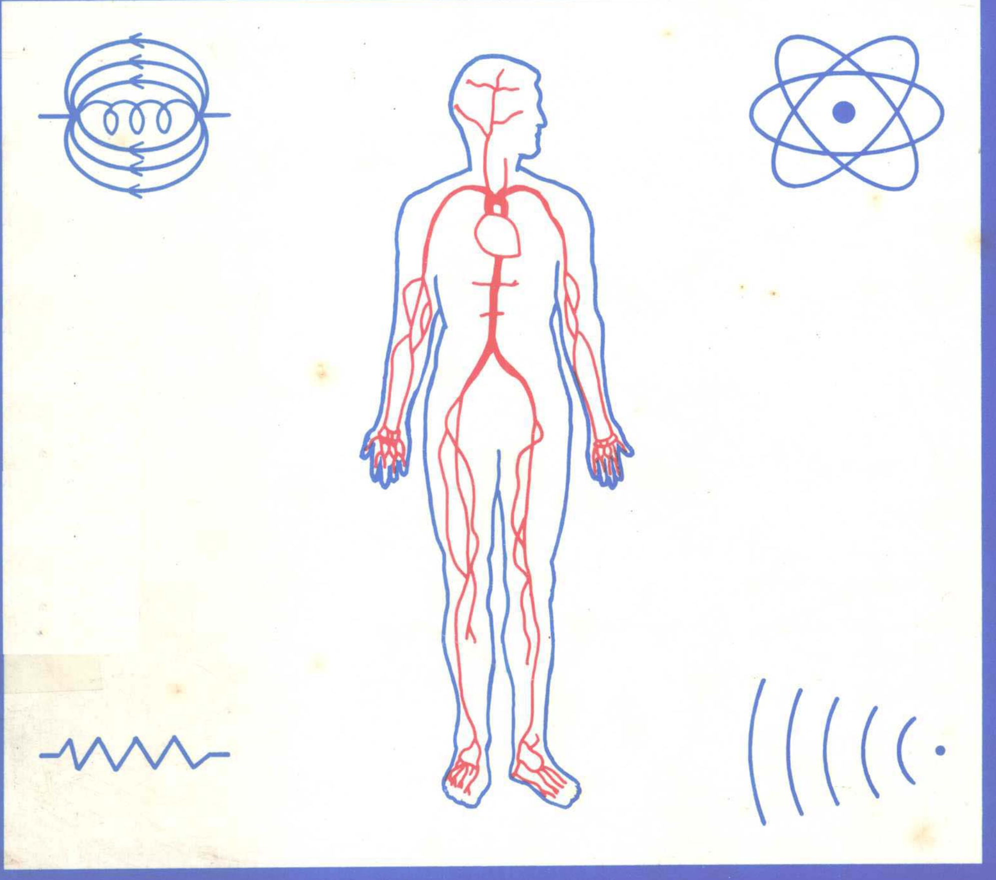
PHYSICS AND THE CIRCULATION

J O ROWAN



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Physics and the Circulation

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in collaboration with the
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Preface

This book aims to outline for the benefit of physicists, engineers and clinical scientists the basis of the wide range of techniques which are involved in the investigation of the circulation of blood in the human body. It attempts to demonstrate the necessity of studying the circulation against a background of fundamental physics.

The first chapter discusses the general properties of blood and the circulatory system, the second deals with those aspects of hydrostatics relevant to the vascular system and haemodynamics. The next four chapters consider in detail electromagnetic flowmeters, ultrasonic methods, electrical impedance techniques and tracer techniques. The basic principles and the measurement techniques associated with each of the different methods are described, their limitations and potential sources of error are highlighted and their clinical applications discussed.

It is hoped that by including descriptions of all these methods in the one publication, physical and clinical scientists will be able to appreciate better their relative merits and be stimulated into matching the technique to the appropriate clinical application.

J O Rowan

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1 Blood and the Circulatory System

1.1 General Properties of Blood

Eighty per cent of blood is water. Despite the fact that chemical substances and cellular elements are constantly entering and leaving the bloodstream, its general composition is relatively uniform in the higher-order animals. This results from a number of regulatory mechanisms acting in conjunction with a rapid circulation which ensures that any potentially large variations in blood composition, initiated by tissue metabolic processes, are reduced by virtue of the relatively large volume of blood flowing through the organs concerned. The blood flowing round the circulation consists of a pale yellow fluid, the plasma, in which the red cells, white cells and platelets are suspended. The specific gravity of whole blood ranges from 1.055 to 1.065 while that of plasma varies between 1.028 and 1.032.

The functions of blood are primarily concerned with the transport of oxygen, nutrient materials, hormones and anti-infective agents to the body tissues, and with the removal of carbon dioxide and other waste products from the tissues and their excretion from the body. Fluid distribution throughout the body also depends on blood flow. Flow of blood through the circulation is maintained by the arterial pressure which results from the pumping action of the heart.

1.2 Coagulation of Blood

Blood coagulates within a short time after leaving the blood vessels and this property has a significant influence on the external examination of blood and its constituents. If blood is withdrawn from a vein in the arm and transferred to a test tube at room temperature it will clot in about five minutes. If steps are taken to prevent the blood from coming into contact with tissue fluid or other materials which it can 'wet', the clotting process is delayed. Thus cannulae manufactured from perspex or nylon coated with silicone are more useful than glass cannulae in which blood clots quickly.

Bleeding times, which are measured by observing the time taken for bleeding to persist after a 4 to 5 mm deep stab wound in the lobe of the ear, are found to be shorter than the coagulation time. The primary factors which contribute to the immediate arrest of bleeding are constriction of the blood vessels and formation of plugs of agglutinated platelets. A vasoconstrictor substance is liberated when platelets disintegrate. Subsequently clotting occurs within a few minutes. Approximately 30 minutes later, when the capillaries tend to re-open in response to the accumulation of tissue metabolites, a blood clot will have sealed the area and the arrest of bleeding is maintained. At a later stage the clot retracts to form a firm plug which is eventually replaced by fibrous tissue.

1.3 Plasma Proteins

Nine per cent of plasma is solid material, 7% being proteins. Plasma proteins exert an osmotic pressure (around 25 mmHg) which influences the exchange of fluid between blood and tissue. In addition they combine with many different substances to form complexes capable of being carried by the blood to appropriate sites where the active components are released.

There are three main types of plasma proteins: fibrinogen, globulin and albumin. Fibrinogen is the precursor of the fibrin of the blood clot and current evidence indicates that it is formed exclusively in the liver. The viscosity of plasma is largely due to fibrinogen. The globulins classified as α_1, α_2, β and γ globulins have a wide range of molecular weights varying from 90 000 to 1 300 000. They are produced mainly in the liver. All known antibodies, which are essential for the development of resistance to infection, belong to the γ globulin fraction. The albumins which have molecular weights of the order of 68 000 are the most abundant of the plasma proteins and are again formed mainly in the liver. At normal concentrations plasma albumin is responsible for around 80% of the total osmotic pressure of the plasma proteins.

The molecules of plasma proteins are 'sausage' shaped with diameters ranging from 3.3 to 3.8 nm. Their lengths vary in proportion to their atomic weight.

1.4 The Effects of Haemorrhage

The loss of a few millilitres of blood per day over several months has

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no effect on the circulation, although it may eventually lead to anaemia. On the other hand, rapid loss of large amounts of blood has very serious consequences. With a rapid blood loss of 800 ml (about 15% of the total blood volume) a drop in arterial blood pressure is prevented by constriction of arteries and veins. However, the heart rate will increase and the cardiac output will fall. With greater blood loss, for example 30–40% of the total blood volume, a state of shock will be induced.

1.5 Red Blood Cells (Erythrocytes)

Red cells are biconcave discs with diameters of the order of 8.8 μm. They have no nuclei and their structure is such that they can take up an elongated shape in small capillaries—their normal shape is subsequently regained on moving into larger blood vessels. The main function of the red cells is to carry haemoglobin. The properties of haemoglobin allow the carriage of the large amounts of oxygen needed for metabolic activities. In addition its buffering power is an important factor in helping to maintain the constancy of blood pH. If the haemoglobin (around $14.5\ \mathrm{g\,ml^{-1}}$ of blood) were not contained in the red cells but were carried by plasma, blood viscosity would be of such a high value that the circulation of blood would be extremely difficult. Furthermore, haemoglobin is rapidly removed from plasma while the life of a red cell is around 120 days.

There are normally 5×10^6 red cells/$\mathrm{mm^3}$ of blood, i.e. $5 \times 10^{12}\ \mathrm{l^{-1}}$. Since the total volume of blood in the body is of the order of 5 l there are about 25×10^{12} red cells in the circulation. In normal subjects there are variations of 10–15% during the day. If the number of red cells is less than $4 \times 10^6\ \mathrm{mm^{-3}}$ the state is described as anaemia, while if the number is greater than $6.5 \times 10^6\ \mathrm{mm^{-3}}$ the condition is described as polycythaemia. The number of red cells will increase in response to a low value of oxygen tension and this is a common finding in patients with chronic diseases of the lungs. The packed cell volume (PCV ≡ haematocrit) and the mean corpuscular volume (MCV) can be found by first of all carrying out a red cell count from a specimen of blood which is then centrifuged (coagulation is prevented in such a way so as not to alter the red cell volume). The packed cell volume in 1000 ml of whole blood is of the order of 450 ml. The mean corpuscular volume, which is found by dividing this figure by the number of red cells present, lies in the range 78–94 $\mu\mathrm{m}^3$.

1.6 White Blood Cells (Leucocytes)

Unlike red cells, white cells contain nuclei. The number in the circulating blood is very variable but is usually between 5×10^3 and 9×10^3 mm^{-3}. An increase in the number above 10^4 mm^{-3} is called leucocytosis and a fall below 4×10^3 mm^{-3} is called leucopenia.

There are three varieties of white cells: the granulocyte series, the lymphocytes and the monocytes. In the granulocyte series the cell diameter varies from 8 to 12 μm, with lymphocytes the cell diameter range is 7 to 15 μm, while the larger monocytes have diameters varying between 16 and 22 μm. Each type plays some role in the protection of the body from disease.

1.7 The Platelets (Thrombocytes)

The platelets which are 2 to 3 μm in diameter are fragments of cytoplasm and have no nuclei. They have a lifetime of about 10 days in the circulation and there are some 2.5×10^5 to 5×10^5 platelets/mm^3 of circulating blood. The number increases after exercise, haemorrhage and surgery. Blood platelets have adhesive characteristics and stick to foreign substances. This adhesive quality is increased after surgery and this is thought to be a factor in the production of venous thrombosis. As mentioned previously, platelets play an important role in the coagulation of blood and in clot retraction.

1.8 The Circulation

The circulation (figure 1.1) can be considered as two circuits. The systemic circuit carries blood to and from the body tissues, and the pulmonary circuit carries blood between the heart and lungs where it becomes oxygenated before being pumped round the body.

1.8.1 The heart

The human heart, which is a muscular structure, has two upper chambers called atria and two lower chambers called ventricles; each of these pairs of chambers is separated by a thin septum. The walls of the atria are thin in relation to those of the ventricles. A fibrous ring separates the atria from the ventricles and other fibrous rings are situated around the arterial orifices aiding the attachment of the great vessels and associated valves. The heart valves themselves are made up of fibrous tissue and

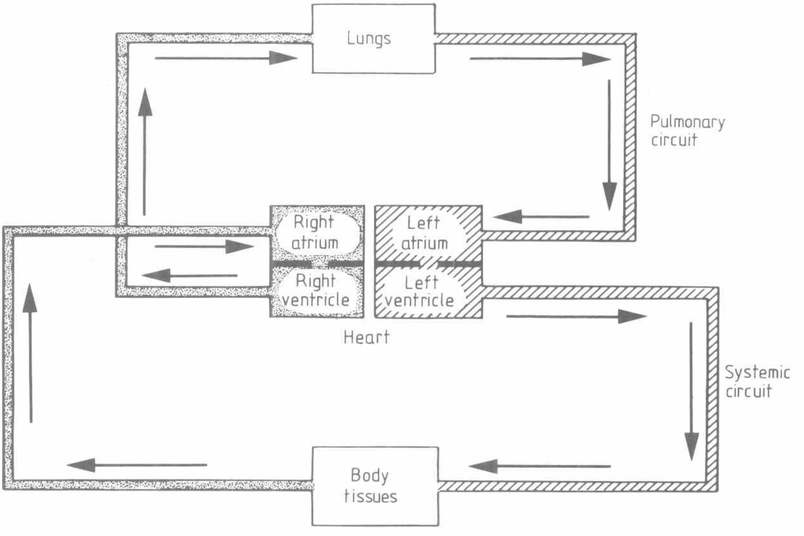

Figure 1.1 Schematic diagram of the circulatory system.

are constructed in such a way as to ensure that blood flows only from the atria to the ventricles and out to the arteries. The points where the veins enter the atria are not provided with valves except in the case of the inferior vena cava which is equipped with a rudimentary type of valve. The atrio-ventricular (AV) valves are structured like sails: between the left atrium and left ventricle two flaps make up the mitral valve while the tricuspid valve with its three flaps is between the right atrium and right ventricle. The arterial orifices are protected by 'semilunar' valves.

The atria have to expend only small amounts of work in transferring their contents to the ventricles, while the ventricles do most of the work of the heart and expel blood into a system of branching vessels which forms a flow resistance network. Each ventricle expels the same amount of blood at each contraction. The heart muscle itself is supplied by blood by the right and left coronary arteries which come from the aorta. Almost 4% of the output from the left ventricle passes into the coronary vessels. The corresponding venous blood passes mainly into the coronary sinus which opens into the right atrium. The coronary circulation is unusual in that blood in the coronary sinus contains only some 5.9 ml of oxygen per 100 ml of blood. The oxygen consumption of cardiac muscle can therefore be increased only by an increase in blood flow.

Anoxia, for example, produces dilation of the coronary blood vessels and an increase in blood flow as great as 500%. In this situation it is assumed that anoxic muscle fibres liberate a vasodilator substance. When the arterial blood pressure falls the coronary blood flow is maintained by an autoregulatory process.

Both atria contract simultaneously and expel their contents into the ventricles. After a slight pause, right and left ventricles contract simultaneously expelling their blood into the pulmonary artery and aorta respectively. Ventricular contraction (systole) is then followed by a pause, referred to as diastole, during which time all components of the heart relax.

The normal heart rate range is 50 to 100 beats/min although normally the mean heart rate for men is 78 beats/min and for women 84 beats/min. With increasing exercise the heart rate increases up to some 200 beats/min, but in trained athletes this increase is considerably reduced. The time taken for the heart rate to return to normal levels after exercise can be taken as a measure of physical fitness, a normal time being of the order of 2 min. The heart rate is increased during emotional stress but falls progressively during sleep; thus, the difference in heart rate between waking and sleeping has been used as an index of emotional tension. Finally, for each degree Celsius rise in body temperature the heart rate increases by about 20 beats/min.

1.8.2 The systemic circuit

The contraction of the left atrium drives blood into the relaxed left ventricle through the mitral valve causing a small pressure rise in the ventricle. As the atrial contraction is ebbing, the left ventricle suddenly contracts producing a very rapid rise in pressure in that chamber. The flaps of the mitral valve are thus brought together by the rising intraventricular pressure and, in addition, brought even closer together by the reduction in the diameter of the fibrous ring to which it is attached. The ventricle remains a closed cavity for a short time until the intraventricular pressure rises above that in the aorta. The aortic valve then opens and there is a rapid pressure increase in that vessel. Initially blood is ejected rapidly into the aorta and then subsequently the rate of ejection decreases. Approximately 0.3 s after the commencement of systole the ventricle relaxes, the intraventricular pressure falls rapidly and the aortic valve is closed by the higher pressure in the aorta. The distension of the aorta resulting from the ejection of blood from the left ventricle causes the blood vessel to oscillate at its natural frequency.

The initial oscillations, called the dicrotic wave, can be clearly seen on pressure waveforms obtained from the direct measurement of arterial blood pressure. When the aortic valve closes, intraventricular pressure falls rapidly until it is less than atrial pressure at which point the mitral valve re-opens.

Blood flows from the veins to the right atrium because the intravenous pressure is higher than that in the atrium. If the capacity of the vascular system exceeds the ability of the heart to fill it, caused, for example, by excessive dilation of the blood vessels, the venous return is greatly reduced with the result that cardiac output and blood pressure drop and the patient loses consciousness.

The pressure inside the chest, the intrathoracic pressure, is negative with respect to atmospheric pressure in normal circumstances. This reduced pressure acts on the large veins and atria. The intrathoracic pressure becomes even more negative during inspiration and the right atrial filling pressure becomes higher, aiding the return of blood to the heart. In other words, the system acts like a respiratory pump. The return of blood to the heart is also helped by muscle contraction, particularly in the lower limbs. On muscle contraction blood is forced out of the capillaries and small veins into the larger veins where valves prevent reverse flow, and the blood returns to the heart.

All blood vessels have a smooth inner lining which consists of flattened endothelial cells, and in arteries this endothelial layer is surrounded by an elastic layer. The two layers together are referred to as the inner coat. This inner coat is surrounded by smooth muscle fibres forming the middle coat which is itself surrounded by the external coat, which is made up of connective (fibrous) tissue. The muscle fibres of the middle coat are reinforced by a network of elastic fibres. The outer coat, too, has a proportion of elastic fibres. Large arteries contain a greater amount of elastic tissue in their walls than do smaller arteries (the arterioles, the smallest arteries, have almost entirely muscular coats). As the vessels become smaller in diameter the total cross section of the vascular system increases. However, under normal conditions a significant number of the smallest vessels are closed. The greatest drop in blood pressure occurs across the arterioles which offer a large resistance to blood flow. Because of this high resistance the pressure in the capillaries is largely independent of the pressure in the large arteries. On the other hand, capillary pressure is affected considerably by the venous pressure since little resistance to flow between capillaries and veins exists. Nevertheless, the capillary bed is capable of exerting substantial influence on the level of arterial pressure because it can accommodate more than the total blood volume. The intermittent input which the arteries receive from the heart is converted to a steady outflow from the capillaries. The circulation of blood transports substances in solution to and from the capillary bed—it is at this level that exchanges between blood and tissue take place. The capillaries have diameters of the order of 10 μm, have no muscular coat and connect arterioles and venules. Clearly, for the blood to circulate, the pressure in the capillaries must be lower than that in the arterioles but greater than that in the small veins.

In general, veins contain valves which ensure that the flow of blood is towards the heart. They have thinner walls than arteries but have correspondingly greater internal diameters. Whereas arteries can withstand considerable increases in pressure with a relatively small increase in volume, veins are easily distended. Nevertheless, although they are distensible and have little muscle in their walls, veins do have a resting tone and can constrict and dilate. Owing to the action of baroreceptors, venoconstriction can be produced by an increase of venous pressure in the right side of the heart, resulting from cardiac failure, and also by a decrease in arterial blood pressure. The amounts of certain chemical substances circulating in the blood can also affect vein diameter. Both adrenaline and noradrenaline, for example, constrict veins. Except in regions close to the heart, the flow of blood in the large veins is continuous. Variations in atrial pressure can be deflected backwards into the adjacent great veins since they do not possess valves. It is possible therefore to detect a venous pulse in normal subjects in the internal jugular vein at the root of the neck.

The difference between systolic and diastolic pressure (the pulse pressure) depends on the characteristics of the blood vessel walls. When the walls of the large arteries become rigid and inelastic the ejection of blood from the left ventricle is less easily accommodated and there is a considerable increase in systolic pressure with each ventricular contraction leading to systolic hypertension. The pressure in the atria and large veins varies with the cardiac cycle, respiration and the position of the subject.

1.8.3 The pulmonary circuit

The pulmonary arteries carry non-oxygenated blood from the right ventricle of the heart to the lungs, while the pulmonary veins carry oxygenated blood from the lungs to the left atrium. The bronchial arteries supply arterial blood to the lungs from the aorta but this

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