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THE PULMONARY CIRCULATION—BEFORE AND AFTER HARVEY*

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The literature of the pulmonary circulation alone is now so vast that all I can hope to do is to give a brief review of some of its more important practical aspects.

Anatomy of the Pulmonary Blood Supply

The advances made in the surgery of the thoracic organs have focused attention on the gross and minute anatomy of the lung and its vascular supply. Dr. W. Snow Miller (1937) has published a most valuable and beautifully illustrated book on this subject which it is a joy to study. He points out that the pulmonary artery in branching follows the subdivisions of the bronchial tree. At first the artery and the bronchus are about equal in diameter; but the subdivisions of the artery get smaller than the bronchi, and at the lobule the artery is only one-fourth or one-fifth the size of the alveolar duct. Here it divides into as many branches as there are alveoli. Each alveolar artery breaks up into branches to supply the air sacs, and these in turn divide to supply the air cells, there subdividing to form the capillary network, the richest and finest in the body, though the capillary meshwork is coarser in the air cells beneath the pleura and in those abutting on connective-tissue septa. The capillary network is so placed that it has air on both sides. The pulmonary veins, in contrast with the arteries, do not accompany the bronchi and are placed as far from them as possible.

The bronchial arteries have been the subject of much research. They vary in number and in their place of origin. In the lungs they enter the peribronchial connective tissue and divide with the bronchi as far as the smaller bronchioles, where they cease. The question of anastomosis between the pulmonary and bronchial arteries has been much discussed. It is generally agreed that there is no anastomosis between the arteries, but that there is direct communication between the capillary systems and that the blood from the bronchial artery is in part returned by the pulmonary veins. Miller has shown that the bronchial arteries also supply the vasa vasorum of the pulmonary artery. Miller states that wounds of the bronchial artery are much more fatal than those involving branches of the pulmonary artery, owing to the higher blood pressure. The problem of this connexion between the two vascular supplies has been studied experimentally in animals. Berry, Brailsford, and Daly (1931) confirm that there is a functional anastomosis

between the two systems, but only through the capillaries, and state that changes in bronchial arterial pressure can lead to changes in pulmonary arterial pressure and pulmonary venous flow. They point out that this vascular shunt must not be forgotten in considering the hydrodynamics of the pulmonary circulation.

It is well known that there are no valves in the pulmonary veins. At the same time the supply of blood to the right side of the heart is greatly aided by the efficient action of the valves in the jugular and subclavian veins, and by those in the veins from the lower extremities in maintaining the filling of what Keith has called the "venous cistern." This comprises the superior and inferior venae cavae, and the innominate, iliac, hepatic, and renal veins, the total capacity of which he estimates as 400 to 500 c.cm. This cistern is subject to the aspirating effects of the inspiratory movements, and is also further fed by the pumping or "milking" effect of the limb muscles when they are in action.

Changes in the Blood in the Pulmonary Circuit

The change in colour from venous to arterial blood was known to the earliest observers, and certainly to Galen, but the actual demonstration of the cause of the change was slow in achievement, and not complete until Lavoisier's researches.

The investigation of the gaseous transfer in the lungs between the blood and the alveolar air redounds again to the credit of English physiologists—notably the Haldanes, the Barcroft, and their pupils—though they are among the first to acknowledge the achievements of Continental and American authorities, particularly Bohr, Henderson, Krogh, van Slyke, and Zuntz. The factors influencing these exchanges are of great interest. In the first place we may consider the extent of the capillary surface in the lungs and the manner in which this is exposed to the alveolar gases. It is estimated that there are about 700,000,000 alveoli in the human lungs, and that the blood is exposed to these gases over an area of 90 square metres (roughly about 1,000 square feet). The surface to which the 3,000 c.cm. of air in the lungs in the condition of moderate distension is exposed is clearly enormous. It is estimated by Maximow that the total area of the capillaries in the alveolar walls is 140 square metres. These figures must of necessity be to some extent conjectural and at best approximate, but in any case they give some idea of the possibilities of exchange between the blood in the capillaries and the alveolar air.

* The Harveian Oration (abridged), delivered to the Royal College of Physicians of London on December 15, 1939.

At rest in man about 250 c.cm. of oxygen is absorbed and about 200 c.cm. of CO_2 is given out per minute. Loewy and Zuntz calculate that under the conditions of gas pressure in the lungs 6,100 c.cm. of oxygen could be absorbed per minute, which gives some idea of one aspect of the enormous safety margin of the pulmonary functions.

A further demonstration of the efficiency of the mechanism for gaseous exchange is afforded by the observation that during exercise venous blood may contain only 5 c.cm. of O and up to 65 c.cm. of CO_2 per 100 c.cm.; yet in arterial blood coming from the lungs the gaseous content is restored to the levels in the resting state, although the actual time the blood is in the pulmonary capillaries is one second or less. In that brief time the blood becomes 95 per cent. saturated with oxygen. Another interesting fact is that the diffusion constant for carbon dioxide is from twenty to thirty times greater than that of oxygen, and Haldane has shown that the oxygen reaching the blood helps to drive out the carbon dioxide. He has also revived a suggestion, originally made by Ludwig, that the alveolar walls may exert some direct influence other than physical on the gaseous exchange. He has brought forward some evidence that this may be of a secretory nature in regard to oxygen. This claim has been adversely criticized by Barcroft and other physiologists.

When it is realized that with violent muscular exertion the gaseous exchange is increased tenfold or more it becomes obvious that there must be some rapidly acting adjustments by which more blood can be passed through the lungs and exposed to the alveolar air when necessary. It is estimated that at the height of inspiration the lungs contain about one-twelfth of the total blood of the body, and that in expiration this is reduced to one-fifteenth or even one-eighteenth, while with increased heart rate the amount may reach as much as one-fifth. An even more striking illustration of the adaptability of the pulmonary circuit is afforded by the study of the cardiac output under varying conditions. It is calculated that at rest the stroke volume of the heart is about 70 c.cm., and the output per minute about 5 litres; this may be increased on exercise to 30 litres. As the total volume of blood in man is roughly 5 litres, it means that the heart can circulate this full amount six times in one minute when the activities of the body demand it, a remarkable tribute to its efficiency as a pump.

The Lungs as Blood Depots

Barcroft (1934) defines a blood depot as an organ which can, and at times does, contain a large quantity of blood capable of being diverted for use elsewhere. One of the first organs he studied was the spleen, which supplies extra blood to the right auricle on exertion. The lungs have been much discussed as possible depots. As we have seen, Malpighi suggested they were designed "as if for a storehouse of blood." Magnus in 1930 and Hochrein and Keller in 1932 came to the conclusion that the lungs served as a blood store, and Sjöstrand in the same year brought forward experimental evidence in favour of this view.

The circulation has been observed microscopically in the mammalian lung by Hall in 1925 and more recently by Wearn and his collaborators (1934). The results obtained are of great interest, especially as supporting the depot function of the lungs. Wearn found that the flow in the arterioles was sometimes pulsatile, more often steady, but frequently changing from one to the other.

The corpuscle content of the plasma in an arteriole may vary from being closely packed to single file. Spontaneous reversal of direction of current may be seen in arterioles. After adrenaline an arteriole with red cells in single file dilated and allowed eight or more abreast. Spontaneous opening and closing of capillaries was common. These experiments afford some idea of the capillary reserve of the lungs, since the number of capillaries through which blood is flowing at a given time may obviously be only a small fraction of the total. The changes in the capillary patterns in the lungs would therefore appear to be kaleidoscopic in their variety.

It has recently been shown by Howell and Donahue (1937) that the blood in the pulmonary artery is richer in blood platelets than that brought to the lungs by the pulmonary veins. They have found megakaryocytes in the lung tissue, and thus demonstrated another function in which the lungs seem to act reciprocally with the spleen. Other activities which have been accredited to the lung are the capacity to destroy lactic acid (Eppinger) and activity in the metabolism of fat (Roger).

Mechanics of the Pulmonary Circulation

The first attempts to study the pulmonary blood pressure in animals were made in 1852 by Beutner under Ludwig's direction. Fredericq improved on Beutner's method. Chauveau and Marey's classical observations on intracardiac pressures were recorded in 1863.

Our knowledge has been greatly extended by Tigerstedt, Wiggers, Hochrein, Daly, and Starling, whose experimental genius stimulated many co-workers. I can only refer to the barest details of some of the more important results, especially those of immediate practical significance. Wiggers (1921) estimates the systolic pressure in the pulmonary artery under normal conditions as varying between 60 and 32 mm. Hg, with an average of 44 mm.; the diastolic pressure ranging between 21 and 6 mm., with an average of 12 mm. Matthes and Hochrein give closely similar figures—namely, average systolic 49 mm. and diastolic 12 mm. Hg. It is noteworthy that the pulse pressure is therefore about 30 to 34 mm. Hg; in other words, it is much more than the diastolic pressure. Another important point is that the average pressure in the pulmonary artery is about one-sixth of the aortic pressure.

The pressure in the pulmonary veins at their junction with the left auricle is assumed to be at or near atmospheric pressure and certainly slightly more than that in the auricle. The capillary pressure is also a matter of assumption. It must be less than the minimum diastolic pressure of 5 mm., and is probably between 3 and 5 mm.

The short course of the pulmonary artery and of its two divisions, together with the rapid subdivision of the intrapulmonary branches to form a quickly widening course on the arterial and capillary side, as well as the shorter extent of the whole circuit, serves to explain the lower pressures and greater velocity of the blood in the pulmonary circulation. Wiggers points out that variations in pulmonary pressures depend upon three factors—the output of the right ventricle, the changes in resistance and capacity in the pulmonary circuit, and "back-pressure" effects from the left side of the heart. This "back working," recognized by Hope but denied by Mackenzie, is now generally accepted by cardiologists as a very important factor in circulatory failure in disease.

The difficult problems of the double circulation become slightly clarified if it is realized that in health the output of the two ventricles per beat must be equal, except for

brief periods of adjustment, and that the systemic circulation can only be effective if the left ventricle is adequately supplied from the lungs, while the right ventricle can only deliver the varying quantity needed if the venous return is effective and adequate, which in turn depends chiefly upon the efficiency of the systemic circulation—the *vis a tergo*, a factor which was recognized by Lower and thoroughly understood by Hope. The adequate filling of the right side of the heart is therefore a primary essential for an efficient circulation; in other words, it is the right or weaker side of the heart which calls the tune and in some senses sets the pace.

An important factor in the adjustment of the two circuits is the great capacity of the lungs to accommodate extra blood, storing it temporarily and passing it on to the left side of the heart as needed. In this connexion it is interesting to note that ligation of one pulmonary artery causes only a temporary rise of pulmonary pressure, and one lung is capable almost at once of dealing with the blood that formerly went to both—a matter of vital importance in connexion with such operations as lobectomy or unilateral pneumonectomy. Another proof of the reserve of the pulmonary mechanism is afforded by the researches of Dunn, who showed that considerable areas of the pulmonary circulation could be blocked by artificial emboli with no more than a temporary fall of pulmonary blood pressure.

The time relations of the pulmonary circulation in man have been studied by Blumgart (1931) and his associates by ingenious methods. The total circulation time from arm to arm varies from twelve to twenty-four seconds, with an average of eighteen seconds; the time from arm to heart, two to fourteen seconds, with an average of 6.6 seconds; and the "crude pulmonary time," five to seventeen seconds, with an average of 10.8 seconds. These methods are proving of clinical application and value, since the pulmonary time is greatly increased in cases of pulmonary venous engorgement.

Control of the Pulmonary Circulation

Since the heart is a double pump maintaining two circuits, separate yet mutually dependent, the two primary essentials for its efficient action must be adequate filling of the right ventricle and effective force of the heart muscle, each factor controlled and regulated to supply the varying needs of the different organs and tissues. It is not surprising, therefore, that mechanical factors play an important part in its control. The filling of the right side of the heart depends upon an adequate pressure in the great veins. The main factor in this is sufficient force on the part of the left ventricle, the *vis a tergo*, transmitted through the capillaries and veins. This is greatly aided by the effect of the respiratory movements on the intrathoracic pressures, constituting what Leonard Hill has called "the respiratory pump," which serves to assist in supplying the venous cistern and in promoting the effective filling of the right heart in diastole. It has been suggested by Eppinger that from 6 to 25 per cent. of the total volume of the venous input is due to this pumping action of respiration. It is well known that there is a rise of the systemic blood pressure with inspiration, though this is slightly delayed. It is therefore at first sight surprising that there is a fall of blood pressure in the pulmonary artery with inspiration, due, according to Sharpey-Schafer and Daly, to diminished peripheral resistance in the lung when it is moderately expanded. Cloetta explains this as being due to the radial traction of the alveoli on the vessels.

Variation in the degree of filling of the right side of the heart is the chief factor in adjustment, alteration in the rate of the heart being secondary to it and effected by reflex nervous mechanisms. Wiggers states that the right auricle contracts a fraction of a second before the left. The manner of the passage of the blood into the ventricles is interesting. In the early period of diastole filling is rapid because the pressure in the ventricle as it relaxes is low; then there is a period of slower entry of blood because the pressures in the veins and ventricle are nearly equal; then there is the short auricular systole, which is said to be responsible for from 20 to 35 per cent. of the ventricular contents.

It is now generally accepted that the rhythm of the heart is myogenic, and that the pace-maker is the sino-auricular node. As long ago as 1881 Ludwig and Luchsinger affirmed that tension inside the heart is a powerful stimulus to its rhythm. Starling by his brilliant researches elaborated this into his well-known "law of the heart." In his Harveian Oration he propounded that "the energy of contraction is thus a function of the diastolic volume of the heart."

Nervous Factors

These are complex but of great interest, since they are for the most part automatic and are brought into play chiefly by the pressure changes in the heart and in the vessels. One of the most dramatic of these is the "Bainbridge reflex." In 1915 Bainbridge demonstrated that increased pressure in the right auricle brought into action a reflex mechanism accelerating the heart rate. This has been shown to be due largely to diminished vagus inhibition, but also in part to increased cardio-accelerator action. A corresponding mechanism on the systemic arterial side was demonstrated by Hering in 1924. He showed that increase in the pressure in the carotid sinus caused slowing of the heart and a fall in blood pressure. This has proved to be due partly to increased vagus inhibition and partly to diminished accelerator action. It is now known that similar reflexes are activated by pressure changes in the aorta and in the heart itself. These are believed to be put in action by "stretch receptors" in these situations, and the afferent paths are through the glosso-pharyngeal and depressor or aortic nerves. It is evident that this is the basis of Marey's law (1859) that a rise of blood pressure tends to slow the heart.

Recent researches by Heymans and other Belgian investigators indicate that changes in blood pressure can by similar reflex paths in these same nerves influence the rate of respiration, a fall of blood pressure stimulating respiration.

Vasomotor Supply to the Pulmonary Vessels

The lungs were supposed to be free of vasomotor nerves until Brown-Séquard in 1871 demonstrated their existence. Even then these results were much questioned. Important work in this connexion was carried out in this country by Bradford and Dean, and in 1890 Dr. James Andrew in his Harveian Oration referred to their results. Later Sharpey-Schafer and McDowall, and more recently Daly and Euler, have investigated them. There seems no doubt now that there is a definite and effective vasoconstrictor supply through the sympathetic system. Hochrein and Keller suggest that its chief use is to subserve the "shunt" activities of the pulmonary vessels in regard to its reservoir or "depot" function. The existence of vasodilators is still in doubt, though the evidence supports the view that there is a parasympathetic supply of this nature.

It seems certain that the pulmonary capillaries are not passive tubes. They undergo active changes in calibre, as observed by Krogh (1929). I have already referred to these as actually seen by Wearn and his collaborators. It was at first supposed that these variations were due to the contractile cells in the capillary walls described by Rouget in 1873. Changes in surface tension in the capillary walls have also been regarded as responsible. These explanations must be considered as doubtful, and there is accumulating evidence that the changes are due to nervous and chemical control.

Little is known of vasomotor supply to veins, but there seems some reason to believe that they have a vasomotor supply and that they may be influenced by the reflex mechanism of the carotid sinus.

Chemical Factors in Regulation

The suggestion that the action of the vasomotor nerves might be due to an adrenaline-like substance liberated at the nerve endings was made by T. R. Elliott in 1904. Cannon subsequently called the substance "sympathin." Loewi in 1921-6 revived and greatly extended this conception of humoral transmission, and it has been studied in this country by Dale and his collaborators with very interesting results.

It would seem in general that the sympathetic endings are activated by an adrenaline-like substance, and are therefore called "adrenergic," while the parasympathetic endings and the motor nerve endings in voluntary muscle are susceptible to acetylcholine, and are therefore called "cholinergic." It is difficult to determine the effects of adrenaline and acetylcholine on the pulmonary vessels because of their coincident effects on the heart and the systemic and coronary vessels. Adrenaline can constrict the pulmonary arterioles and raise the pressure in the pulmonary artery, but it can sometimes produce dilatation, though this effect is apparently more marked in the capillaries. The action of acetylcholine varies with the dose, a dilatation of the vessels occurring with small and a constriction with large doses.

Histamine is normally present in the lung. Its effect is different upon the pulmonary vessels, which it constricts, from that on the systemic, which it dilates. The part played by Sir Henry Dale in the investigation of the problems of humoral transmission it would be difficult to overestimate. It was recognized by the award of the Nobel Prize in 1936. These researches illustrate the paramount importance biochemistry is taking on in the elucidation of physiological and pathological problems.

Adjustments of the Two Circulations

Although the two circulations are so closely dependent on each other there is a remarkable independence in regard to the respective arterial pressures in health. Considerable rises can take place in the systemic arterial pressure with little or no effect upon the pulmonary pressure levels, and the lungs can undoubtedly protect the left side of the heart from overdistension by shunting large quantities of blood into the pulmonary veins and capillaries. It is only when the left ventricle fails that the "back-working" effects become serious, increasing the pulmonary pressures, and decreasing the velocity of flow while increasing the right ventricle contractions and engorging the lung.

I have endeavoured to give a very brief description of the imposing edifice which has been built by Harvey's successors on one part of the foundation he laid so successfully. There is still much to be done, and no doubt

some parts to pull down and rebuild. We must always keep open minds and be prepared to modify and adapt as new facts come to light.

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NOTES ON PENETRATING CHEST WOUNDS

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The following notes are based on over six hundred cases treated at base hospitals in France and England in 1917 and 1918. They may prove of some value to a new generation of medical officers who will presumably be called upon to treat large numbers of similar cases in the immediate future.

The following table shows the relative frequency of the various complications occurring either singly or in combination in a consecutive series of 250 cases seen at an advanced base hospital in France. Of these 75 per cent. were admitted during the first week and 90 per cent. within fourteen days of being wounded.

	No.	Per cent.
Haemothorax and pneumo-haemothorax:		
Simple	143 (57.2%)	
Infected	39 (15.6%)	182 72.8
Empyema (without obvious haemothorax) ..	9	 3.6
Pneumothorax (without obvious haemothorax) ..	3	 1.2
Pleural effusion (simple)	3	 1.2
Homolateral collapse (deflated lung)	24	 9.6
Contralateral collapse	16	 6.4
Bronchopneumonia and capillary bronchitis ..	10	 4.0
Lobar pneumonia	7	 2.8
Pericarditis (purulent)	2	 0.8
Septicaemia	2	 0.8
Mediastinal abscess	1	 0.4
Tetanus	1	 0.4
Deaths from all causes while under treatment	12 (4.8%)	
Transferred to England	238 (95.2%)	

Twenty-four cases of non-penetrating wounds or wounds in which penetration was doubtful are included in this series because in all such cases injury involved either the lungs or pleura, as shown by haemoptysis, pleurisy, or pulmonary collapse. Cases seen at a later stage (over 350) at a base hospital in England are not included in the above list, as certain temporary complications—for example, collapse of lung—would have disappeared before the patients came under observation.

The after-history of cases which survive to reach the base emphasizes the great difference in outlook between wounds caused by bullets and those produced by fragments of shell. A simple "e. and e." wound from a machine-gun or rifle bullet which drills a clean hole through clothing, chest wall, and lung substance but fails to penetrate the heart or a big vessel causes remarkably few symptoms after the initial shock and rarely produces sepsis. Apart from temporary haemoptysis and haemothorax—which, unless large, is better left alone—the patient suffers relatively little inconvenience and rapidly