THE CLINICAL PHYSIOLOGY OF THE LUNGS

By

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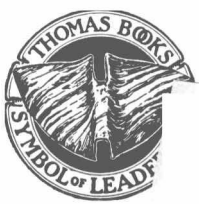

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To

K. R. D.

In grateful recognition

of her assistance

in the preparation of this book

PREFACE

A SERIES of lectures which I gave in 1944 on pulmonary edema and inflammation resulted in the publication of a small monograph (1).* They resulted, too, in systematizing and clarifying my ideas concerning a number of clinical conditions frequently met, but, because of the highly specialized structure and function of the lungs, hard to understand. The lectures recounted research experience and correlated material which went back to 1921, when, at the request of Francis W. Peabody, I devised and, with the help of Herrman L. Blumgart, carried out experiments to demonstrate the readiness with which stasis of blood in the lung capillaries excludes air from the alveoli.

During the ensuing years, aided by many students, I carried on in my laboratory a series of experiments directed at explaining and evaluating physiologically such frequent clinical experiences as obstruction of the pulmonary arteries and veins, the production and removal of transudates and exudates, the entrance of air into the lung capillaries, and other clinical problems. All of the numerous experiments were performed on anesthetized animals. They necessitated the creation of new methods for exposing and cannulating the different pulmonary vessels, for separating and collecting air from the two lungs, and other technical procedures hithertofore accomplished only upon animals with open chests and under artificial respiration—very different physiological conditions from those existing in naturally breathing animals with closed chests.

These efforts seem labored and artificial compared with techniques available today, when catheterization of heart and blood vessels is readily accomplished in animals and in man, and without the necessity for anesthesia. Yet I believe the results we attained have been perfected, not superseded, by this later work.

It was my purpose in a second series of lectures, given during

See References, Chapter I.

the spring of 1950 at The Medical College of the State of South Carolina, to extend what I had presented in 1945, utilizing for this purpose data obtained by many investigations during and since the war on animals and on man. These lectures, in their turn, I have assembled and amplified into the present monograph; and since much of the material presented is under active discussion and research, I have tried to write informally and suggestively, as is appropriate to an effort designed to give impetus to thinking.

In planning the lectures, I was guided by what I considered the basic structural components of the lungs for accomplishing the constant adaptations which occur during breathing. One begins, naturally, with the arteries; then considers the veins and capillaries; next the bronchioles; the nerves; and, finally, the lymphatics.

I have avoided discussion of gas exchange, except in so far as it applies directly to our problem. This may be an error; but an attempt at its consideration would extend unduly my primary objective of considering adaptive reactions in the lungs themselves, and not the effect of these reactions on the whole body.

It is my experience that, as a person grows older, he develops a wholesome reluctance to speak about subjects still very much under judgment and research, unless fortified by personal efforts in the field. For what follows you may be sure I can say with old Ulysses, as he reviewed the past, "I am a part of all that I have met."

Falmouth, Massachusetts CECIL K. DRINKER

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THE CLINICAL PHYSIOLOGY OF THE LUNGS

I

THE PULMONARY ARTERY AND ARTERIOLES

INFARCTION. INHERENT REGULATION OF BLOOD FLOW

The Pulmonary Artery and Arterioles

THE PULMONARY artery arises from the left side of the base of the right ventricle and passes up and back for about 5 cm., to divide into right and left branches. The diameter of the main trunk averages 30 mm., slightly greater than that of the aorta. The wall of the artery is comparatively thin, with elastic tissue the main structural component. This is also true of the branches. Smooth muscle is, of course, present and is proportionally greater in amount in the small vessels; but the dominance of elastic tissue throughout the system is most important. Macklin (2) has demonstrated that the bronchi lengthen with full inspiration; and, since the arteries accompany the bronchi closely, it is essential that they follow bronchial changes smoothly—a correlation which could not readily occur were the arteries the highly muscularized tubes we find in the systemic circulation. The pulmonary artery and its branches are supplied by both vagus and sympathetic nerves, but, so far as definite effects resulting in contraction are concerned, these are apparently of little consequence, and are probably mainly afferent.

In considering the regulation of blood flow through the lungs, confusion has arisen from facts which characterize the systemic circulation. The systemic circulation is organized as a series of shunts, the objective being to provide oxygenated blood to tissues which are active. Thus, if one passes from rest into physical activity —running, for example—a general constriction of vessels in the abdomen occurs, with a concomitant opening of arteries and capillaries in the muscles. This adaptation is brought about in large degree by nervous regulation. The lungs, on the other hand, are quite uniform in structure. No one part is advantageous over another for providing oxygenation of the blood; and all parts, saving only the walls of the large vessels and bronchi, have an available supply of oxygen

from the alveolar air. Furthermore, the lung tissue is a slight user of oxygen, the diffusion of oxygen and carbon dioxide between air and blood being a process requiring no expenditure of energy. In physiology it is dangerous to use teleological reasoning, but I find it very hard to see what advantage would be offered by centrally controlled reactions of the pulmonary blood vessels which resulted in shunting the blood to one part of the lungs and closing off another. In my view, the integration of the blood flow through the lungs with the needs of the body is achieved by the structure of the lungs themselves, not by any complexity of central regulation.

This does not mean that the pulmonary arteries and arterioles are incapable of contraction nor that the amounts of blood are the same throughout the lung tissue. The blood vessels possess sufficient smooth muscle to bring about constriction and to sustain it against the force of right ventricular contraction. In common allergic states, it is inescapable that the blood vessels are contracted with the bronchioles. In certain animals strong and persistent contractions result from intravenous injections of foreign protein. Thus, if one gives horse serum intravenously to a cat, there is an immediate and extensive rise in pulmonary arterial pressure; and the same sort of reaction accompanies anaphylactic shock in the rabbit and to a lesser degree, in the cat (3). Anoxia, too, causes vascular constriction—at once released on breathing pure oxygen (4). These reactions are apparently direct effects upon the smooth muscle—that is, they are inherent in the lungs themselves and are not dependent upon reflex nervous influences.

In addition to the pulmonary artery and its branches, the lungs possess systemic vessels, the bronchial arteries and capillaries. These supply the bronchi and provide vasa vasorum for the pulmonary arteries and veins. Reactions in this system are probably similar to those in other parts of the body, but do not seem to be so intense.

In a normal man of 70 Kg. (154 lbs.), with a total blood volume of about 6,000 cc., the pulmonary artery, capillaries, and veins contain 500 to 1,000 cc. of blood. This volume fluctuates, becoming greater on inspiration and being uniformly greater when the lungs operate at larger size, as in physical exercise, when the pulmonary blood volume may be one-fifth of the total blood volume, or in the normal man, 1,200 cc.

By virtue of their large capacity and their extreme elasticity, the lungs are an important potential reservoir of blood. Thus, if cardiac inflow is high and the left ventricle becomes unable to expel the large volume of incoming blood as fast as it is provided, blood may accumulate in the lungs, to be slowly emptied out as the heart becomes able to deal with it. One of the handicaps to physical work experienced by patients with emphysema is due to diminution in number of the lung capillaries and loss of lung elasticity, so that the patient is deprived of the beneficent reservoir effect so definitely present in normal lungs.

The pulmonary capillaries offer a vast surface for gas diffusion, about 140 square meters. Three to 5 liters of blood traverse these vessels each minute, and this amount readily reaches 20 liters during hard exercise. It is estimated that each corpuscle passes through the pulmonary capillaries in one second, a figure which must vary markedly in different parts of the lungs at the same moment, but which probably becomes increasingly uniform as cardiac output rises.

Figure 1 is a diagram showing the arrangement of the vessels in a lung lobule. The pulmonary arteries are closely associated with the bronchi, and branch to follow each bronchiole until a respiratory bronchiole is reached and capillary nets begin to appear. The final ramification is over the alveolar surfaces, where the venous net begins. The lung capillaries have scarcely any individual length. They form a close-meshed net, the mesh of which is often less in diameter than the capillaries which form it (Figure 2). Through this net the red cells pass as a thin sheet over the alveolar surface. A network very similar to that in the mammal is found in the lung of the frog, where it may be observed microscopically under very normal conditions.

The blood corpuscles pass through the capillaries usually in single line and often undergo marked deformation as they twist around corners. The elasticity and ductility of the blood cells is ordinarily not realized. If the cells are stiffened even slightly, as by brief immersion in dilute formalin, they at once block the flow of blood and death ensues. The deformation and return of a corpuscle to normal shape are shown in Figure 3 from a motion picture film made by Krogh (5). In discussing the elasticity of the blood cells,

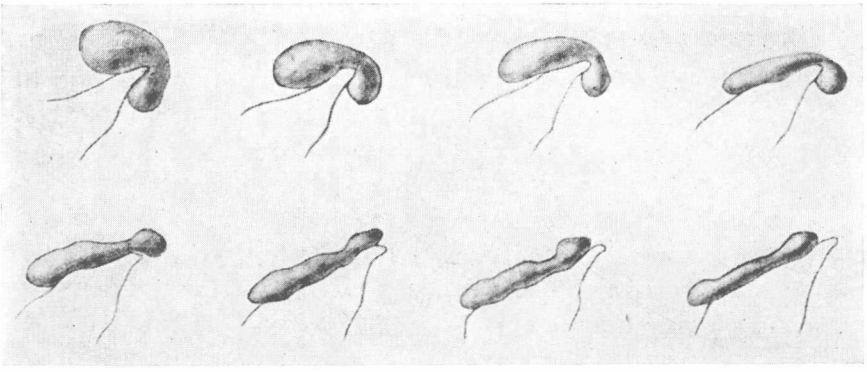

FIGURE 3. The deformation and return to normal shape of a red cell passing through the lung capillaries of a frog. The corpuscle is moving from right to left; the pictures are to be viewed from left to right, beginning in the upper left-hand corner. A red cell is caught upon the edge of a capillary for about 4 seconds. It rides over slowly, and in the last figure, 0.3 second after release, has regained normal shape. From a moving picture film. (From KROGH, A.: *The Anatomy and Physiology of Capillaries,* Fig. 22, p. 61. New Haven, Conn., Yale University Press, 1922.)

Krogh points out that corpuscles frequently pass through filters which hold back far smaller particles, and that this ability to slip through small holes—smaller indeed than the diameter of the cells—is probably an important factor in the passage of red cells through the intact walls of capillaries. This passage of red cells through capillary walls invariably occurs when blood flow in a capillary stops or is much slowed. Little or no pressure is needed to bring it about, and there is no actual hemorrhage as evidenced by masses of cells outside the vessel wall. Corpuscles pass through without permitting leakage of plasma, much as a needle may be pushed through a film of gelatin without in the least affecting the integrity of the film.

The pressure in the pulmonary artery and its larger divisions is not high. Many figures for this are available both in animals and in man. Using catheters passed into the artery, Riley and his associates (6) obtained typical figures for three normal men between 26 and 36 years of age. Mean pulmonary pressures in these men while at rest averaged 13 mm. of Hg; mean brachial artery pressures, taken simultaneously, averaged 84 mm. Hg. Similar measurements have been made by many others. Normal levels must, of course, be estab-

lished, but what interests us far more are measurements of the degree to which the pressure may rise or fall in normal persons during familiar experiences and in subjects with diseases of the heart and lungs. Contrasting with the values for rest, exercise in the three men cited above produced a slight lowering of pulmonary arterial pressure—a mean value of 10–11 mm. of Hg as against 13 mm. at rest. This probably expresses the fact that the pulmonary vascular bed of the normal lung enlarges during increased breathing to a capacity overshadowing the cardiac output, and the lung vessels are thus not subjected to the strain experienced by the less expansile systemic group. If exercise is accompanied by anoxia, as may often be the case, a different result ensues. Motley and his collaborators (7) found that acute anoxia, induced by breathing 10 per cent oxygen in nitrogen for short periods, caused a uniform increase in the mean pulmonary arterial pressure of five normal subjects of from 13.1 mm. to 23 mm. Hg, with a rapid fall to normal when the anoxia was relieved. Pulmonary hypertension occurring as a partial result of anoxia—for example, in extreme exercise—is a frequent experience of man.

Experiments upon anesthetized animals with chests closed and breathing naturally confirm the above finding (8), and have added the fact that inhalation of pure oxygen causes pulmonary arterial pressure to fall, a matter of some importance when considering the effects of oxygen inhalation in cardiac failure and in asthma.

Pulse pressure in the pulmonary arteries is usually higher than the mean pressure, an expression of the very low resistance offered by the lung vessels. All of these reactions are direct effects upon the smooth muscle in the pulmonary vessels. They are thus inherent in the lungs themselves. So too, the regulation of blood flow through the lungs—a flow which changes smoothly with the needs of the individual—is inherent in the general structure of the lungs and in the amount of blood supplied by the right ventricle. It does not depend on nervous effects exerted within the lungs themselves.

There is a point which should be made here. In spite of the great elasticity of the lung vessels, including the capillaries, it is true that when the left ventricle fails to deliver all the blood coming to it—and this is something which occurs briefly in normal persons subjected to excessive physical effort—pressure in the pulmonary artery

rises. The effect is seen in exaggerated degree when cardiac lesions are present or in pulmonary disease, such as chronic emphysema, in which the ultimate distribution of the pulmonary vessels is decreased and the lung elasticity lessened. Riley and his associates (6), for example, report a patient with chronic emphysema whose normal pulmonary artery pressure at rest of 13 mm. of Hg rose to 19 mm. on his sitting up, and to 43 mm. during work.

Finally, alveolar air pressure can cause compression of the lung capillaries and impose varying degrees of resistance. In the dog, an increase of air pressure in the trachea to 80 mm. of Hg completely blocks pulmonary blood flow, and death is prompt.

Interest in breathing oxygen at pressures above atmospheric, in order to secure the highest possible oxygenation of the blood, and in the use of artificial respiration apparatus which pumps oxygen to the lungs with a blast of positive pressure, brings to notice this matter of tolerable alveolar air pressure. It is safe, apparently, even in infants to use positive pressure lung inflation up to 14 mm. of Hg. Possibly a higher limit might be set, but the issue is one which demands conservatism. Let me illustrate. In training for submarine service in the past, candidates were required to escape from a tank simulating a sunken submarine. The trainee wore a device for oxygen breathing with a mouthpiece and nose clip. He inhaled the oxygen naturally and exhaled through a valve in the appliance. In order to qualify for the United States submarine service, trainees were required to escape from depths to about 50 feet. The young men undergoing such tests were in the best of health, yet during our early escape training five deaths occurred. The cause of these accidents was soon discovered. When any normal person puts his face under water he holds his breath tenaciously—a compelling reflex. If, with breath held, a trainee rose 50 feet to the surface, the air in his chest expanded as the pressure was reduced. This took place rapidly; and not only was blood flow through the lungs reduced but air was forced from the alveoli into the lung capillaries, bringing about fatal coronary and cerebral embolism. The remedy was obvious. Trainees must wear the mask near the surface and learn above all else to exhale. I have watched experienced men come up 50 feet exhaling steadily and never taking a single breath from the apparatus. Their breathing was accomplished by the increasing

volume of oxygen in the lungs, which enabled them to dispense with inspiration.

It is thus possible for air in the alveoli to impede pulmonary blood flow and to cause increase in pulmonary arterial pressure. Reciprocally, it is easy to show that overstuffing of pulmonary capillaries, as is seen in cardiac disease, may so splint the alveolar walls and encroach upon alveolar air space as to limit the amount of air which is able to reach the alveoli.

Infarction

One of the best ways to learn something of how the pulmonary circulation is regulated is by study of the events following obstruction of the arteries. The problems of diagnosis and management of pulmonary embolism are much in the foreground today. Methods for treating these cases, whether by administration of anticoagulants or by ligation of veins, appear steadily. But the physiological effects of arterial block in the lungs, and even more the causes of blood clotting in remote and apparently uninjured veins, are poorly or not at all understood. We used to, and still do, fear pulmonary embolism after surgical operations, particularly in the pelvic region. But in recent years we have learned that lung embolism often occurs in individuals apparently in the best of health, causing symptoms which formerly we vaguely called ideopathic pleurisy or pleurodynia.

Given a healthy heart, such as is found in a young adult, it is surprising to realize what large degrees of sudden pulmonary arterial obstruction may be withstood. In 1923 Haggart and Walker (9), in experiments on anesthetized cats with closed chests and breathing naturally, were able to place a clamp, such as is shown in Figure 4, on the pulmonary artery or one of its main divisions. In such a preparation the vessel may be closed by means of the screw, and by reading the scale upon the instrument, one may ascertain the degree to which the vessel is occluded. In Haggart and Walker's experiments if the left branch of the pulmonary artery was clamped, the pulmonary artery pressure—measured by means of a cannula which did not interfere with blood flow—rose for a short time about 29 per cent. This did not cause any significant change in systemic blood pressure nor in cardiac output, and resulted in but moderate