Editorial

The Volume of Blood in the Lungs

"... the lungs are made by Nature as if for a storehouse of blood, so that it may constantly in turns give forth blood to the heart, which, thence driven into the whole body by continual circulation, may impart life and motion to everything."—J. Young; Malpighi's "De Pulmonibus" [1661] Proc Royal Soc Med 23:7, 1929.

INTEREST in the pulmonary blood volume apparently began with Malpighi who noted that inflation displaced blood from the lungs of the frog.1 Many such qualitative observations were made during subsequent years but not until the turn of the present century, and the advent of heart-lung preparations, did quantitative measurements become possible. In the 1920's, the development of the indicator-dilution technique extended the prospect of quantitative measurements to the intact animal and man.

Reasons for the continuing interest in pulmonary blood volume have varied with the times and with the investigators. At present, four main lines of interest may be identified: (1) the role of the lungs as a blood depot, (2) the blood reservoir as the site of stretch receptors, (3) the performance of the congested lung, and (4) the partition of the pulmonary blood volume. All of these lines of interest are apparent in the five papers that have recently been published, or are about to be published in Circulation.2-6

The Lungs as a Blood Depot

The volume of blood in the lungs at any instant depends on the balance between inflow and outflow as determined by the respective actions of the two ventricles and on the distensibility characteristics of the pulmonary vascular tree; variations in the ventilation, in total blood volume, and in systemic vasomotor activity exert considerable influences on the regulation of the low-pressure, highly distensible pulmonary circulation.7 Whether autonomic activity affects the distensibility characteristics is unsettled.8, 9

Traditionally the lung is pictured as a blood depot, operating to ensure an uninterrupted supply of blood to the left ventricle during acute disturbances in venous return, such as those produced by breathing, change in posture, and exercise.2 Another accepted view is that the lungs are at the mercy of the systemic circulation, passively accommodating or yielding blood according to the dictates of systemic vasomotor activity.8, 9 Until recently, accurate measurements of pulmonary blood volume, or reliable indices of a change in pulmonary blood volume, were unavailable to test these concepts. But, during the last 2 years, two new methods have become available.

The first of the new methods, applicable to animals, is the use of chronically implanted electromagnetic flow probes, one around a pulmonary artery and another around a pulmonary vein; a change in pulmonary blood volume at any instant is merely the difference between inflow and outflow.2, 10 Since the electromagnetic flow meter is still in its infancy, further comment will be confined to the second method which uses the indicator-dilution principle to measure the pulmonary blood volume11, 12 instead of "central blood volume," a vague entity that includes not only the volume of blood in the lungs but also in the heart and in an indeterminate portion of the systemic circulation.

For the measurement of the pulmonary blood volume, systemic arterial dilution curves are obtained after separate injections of the test substance into the pulmonary artery and left atrium; from this combination, the pulmonary blood volume is calculated by difference. It should be noted that the volume calculated by the indicator-dilution technique is a virtual rather than an anatomic volume since it only includes blood with which dye has mixed and excludes stagnant and se-

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questered blood. It is true that the virtual and anatomic volumes are probably similar in the normal pulmonary circulation, but there is no predicting how the volumes and their meanings are affected either by drastic experimental conditions or by clinical disorders of the heart and lungs.

Obviously, the combination of right and left heart catheterization is too formidable for regular clinical or investigative use. Also, there is an inherent error in the calculation by difference which is, at best, of the order of 10 to 15%. Nonetheless, this technique has provided a standard of reference for less direct methods, for example, external counting after injection of a radioactive tracer, in which the estimation of mean pulmonary transit time is complicated by uncertainties concerning the exact vascular anatomy viewed by the counter. In normal subjects, the pulmonary blood volume is approximately 10% of the total blood volume, a value almost identical with that established long ago, by direct measurement, in the heart-lung preparation of the dog.

The Blood Reservoir as the Site of Stretch-Receptors

In recent years, stretch-receptors in the intrathoracic portion of the circulation have been postulated as devices for signaling the degree of distention of the atria and venous atrial junctions and for reflexly modifying the vasomotor behavior of the heart, the systemic resistance vessels and the kidney. At present, it seems likely that either different or adaptive mechanisms are operative during acute experimental engorgement and during chronic pulmonary congestion. To explore this important problem further, reliable techniques are needed not only to measure total pulmonary blood volume but also to partition the intrathoracic blood volume for the sake of determining the degree of distention of the consecutive segments of the pulmonary circulation and of the individual cardiac chambers. A preliminary step has been made in this direction and will be considered subsequently.

The Congested Lung

It has long been known that the lungs are stiffened by either acute or chronic engorgement. It has also been appreciated that the diminished compliance of the engorged lung somehow helps to set the breathing pattern and is somehow involved in the genesis of dyspnea. In patients with chronic pulmonary congestion, the distinction between changes in compliance attributable solely to expansion of the pulmonary blood volume and to anatomic sequelae of chronic pulmonary engorgement has not been easy to accomplish either by studies of the mechanics of breathing or by determinations of "central blood volume." But, in general, anatomic changes do seem to reduce further the low compliance effected by pulmonary engorgement and to lead to obliteration of dependent parts of the pulmonary vascular tree. One consequence of the anatomic restriction and the reduced compliance in chronic pulmonary congestion may be a normal pulmonary blood volume despite high pulmonary vascular pressures.

It is difficult to generalize from chronic to acute congestion: In states of chronic circulatory congestion with normal hearts, the lungs seem to share in the expanded total blood volume; on the other hand, in the acute expansion of the total blood volume by infusion, the lungs appear to be spared and the expanded blood volume is accommodated largely in systemic veins.

Partition of the Pulmonary Blood Volume

Interpretations of the behavior of the pulmonary circulation on the basis of pressure-flow measurements have been handicapped by lack of simultaneous measurements of pressure-volume. This is true not only for the entire pulmonary circulation but also for the behavior of the consecutive pulmonary vascular segments.

The first step in establishing the volume of a pulmonary vascular segment was made by Roughton, in 1945, when he used an equation to calculate the volume of pulmonary capillary blood exposed to alveolar gas \(V_c\). The ingredients of the equation were: (1) in-
vitro measurements of the rate of reaction of carbon monoxide with suspensions of human erythrocytes at normal and at high oxygen tensions, (2) in-vivo measurements of the rate of uptake of carbon monoxide at high oxygen tensions, and (3) several reasonable physiological assumptions. He concluded that $V_e$ was approximately 60 ml at rest and 95 ml during heavy work.\(^{19}\)

Subsequently, Boughton and Forster\(^{20}\) provided another ingenious equation which made possible the determination of $V_e$ by fractionating the total diffusing capacity of the lungs as though it were composed of two components, the diffusing capacity of the alveolar-capillary membrane ($D_M$) and the volume of blood in the pulmonary capillaries ($V_c$). Obviously, this approach is an important conceptual advance.\(^4\), \(^5\) But, in practice, especially when applied to patients with heart or lung disease, the $V_e$ is subject to considerable uncertainty: its determination includes all of the opportunities for technical errors that are involved in determining the total diffusing capacity of the lungs for carbon monoxide; the reaction rate of carbon monoxide and hemoglobin has been measured only under certain limited conditions; different modifications of the method for measuring the diffusing capacity introduce new errors; the $D_M$ and $V_e$ are highly sensitive to slight technical errors; the separation of the total diffusing capacity into $D_M$ and $V_e$ based on the kinetics of combination of carbon monoxide with intracellular hemoglobin is somewhat unreliable. These considerations suggest that $V_e$ probably has no sharp anatomic boundaries; that even in normals, this virtual volume may vary with the experimental condition and method; that it is most meaningful when compared under identical conditions in the same subject; and that $V_e$ is most difficult to measure reliably and to interpret meaningfully in those diseases which affect the determination of the diffusing capacity of the lungs.\(^{21}\)

A second step in partitioning the pulmonary blood volume in vivo has recently been proposed by Feisal and associates.\(^{22}\) It involves the combination of indicator-dilution and ether-plethysmographic techniques in dogs to determine the pulmonary arterial blood volume. By this fresh approach the pulmonary arterial blood volume is approximately 20 to 25% of the total pulmonary blood volume. Although this value is somewhat lower than expected on the basis of observations on the isolated lung,\(^{13}\) and this discrepancy remains to be resolved, this approach represents a needed beginning in the partitioning of the pulmonary blood volume in intact animals.

It is clear from the above, that the pulmonary blood volume has been, and continues to be, a subject of lively interest from many different points of view. For a long while the intensity of this interest tended to obscure the approximate nature of the methods used for its measurement. Recently, more accurate measurements of the total pulmonary blood volume became available and the partitioning of the pulmonary blood volume in vivo became an attainable objective. It seems likely that the next few years will see fresh techniques and further clarifications of the physiological and pathophysiological roles of the pulmonary blood volume.

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**References**

Because Bacon and others advocated that the experimental method could best be promoted by the corporate action of natural philosophers, frequent informal and sometimes secret meetings of men of science were held between 1600 and 1650 in various centers of Europe. These assemblies (sometimes referred to as the “invisible college”) were soon to lead to the founding of many great scientific academies and societies. The results of the experiments and discussions, and the other events of philosophical and political importance in the early meetings, were frequently recorded. Copies of the records were then sent as letters to friends engaged in similar activities in other centers. Communication in all countries at that time was facilitated by Latin, the international language of the learned. But the vernacular was also coming into use by natural philosophers.—J. R. PORTER: The Scientific Journal—300th Anniversary. Bact Rev 28: 211, 1964.
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