STUDIES ON THE VELOCITY OF BLOOD FLOW

V. The Physiological and the Pathological Significance of the Velocity of Blood Flow[1]

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The velocity at which blood flows is of considerable consequence in maintaining physiological well being. As has been pointed out in a preceding communication, it is not sufficient that an adequate amount of blood be expelled from the heart per minute; it is of primary importance that this blood be conveyed to the depots of utilization with the proper dispatch, and that it flow through the capillaries at sufficient speed to allow the proper interchange between blood and tissues. It may be contended that whether an adequate volume of blood reaches the tissues through narrow arteries at a great velocity, or through large arteries at a lesser velocity is not of primary importance. A given amount of blood ejected from the heart which might be entirely adequate if supplied through narrow vessels at a high velocity might, however, be inadequate if transported at a low velocity through wide vessels.

We believe, therefore, that both the minute volume output and the velocity of blood flow are indices of two fundamental aspects of the circulation, aspects that are closely related, and which must both be satisfactory if the proper supply of blood to the tissues is to be maintained. The relationship between volume flow and velocity flow through tubes of known diameter is a simple one and is expressed by the equation $V = \frac{A}{\pi r^2}$, where V = velocity expressed in seconds, A = volume per second, and r is the radius of the tube. It is evi-

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dent, therefore, that in a tube of constant cross sectional area, changes in the volume flow will be paralleled by changes in the velocity flow, and that any lack of proportionality must be due to alterations of the cross sectional area. If in a given individual, simultaneous volume and velocity measurements were possible, their parallelism would provide important information on vasomotor and other changes in the functional cross sectional area of the vascular bed. Further discussion of this interesting problem will be deferred until a later communication in which such measurements will be presented, and their significance discussed more fully.

CONDITIONS WHICH AFFECT THE VELOCITY OF BLOOD FLOW

The fundamental characteristics in a hydraulic system which determine the velocity of flow are, of course, well known. The mean velocity of a stream through a rigid tube is directly proportional to its cross sectional area and the difference in pressure from point to point. The product of the cross sectional area multiplied by the pressure head, when divided by the coefficient of viscosity, gives the velocity of flow. This has been expressed, according to Poiseuille's Law by the formula $\frac{(P_1 - P_2)r^2}{8\,LN}$ where $P_1 - P_2$ is equal to the difference in pressure, r is the radius of the tube, L is the length of the tube and N is the coefficient of viscosity. Formulation of the factors by such a law is valuable in so far as it serves to focus attention on the character of the influences which determine velocity, but the futility of exact application of such a law to biological phenomena becomes at once apparent when one considers the constant flux of circumstances within the body. The peripheral vascular bed is constantly varying, not only because of the delicate flexibility of the vasomotor arteriolar control, but also because, as Krogh has shown, certain capillaries may temporarily be entirely or partially closed. It must, morever, be borne in mind that a certain change, such as peripheral vasodilatation, may influence the velocity of flow simultaneously in two and opposing directions. The velocity of flow varies inversely as the resistance, and therefore vasodilatation, by lowering the resistance, tends to increase the velocity. On the other hand, vasodilatation by increasing the cross sectional area of the flowing stream tends to

decrease the velocity. This, and many more continually varying relationships, serve thoroughly to confuse theoretical formulations. It is by such "vasomotor breezes," as Allbutt has termed them, that application of the abstract laws of theoretical physics is confounded; for, whether one or another factor predominates or, whether by chance they counterbalance, cannot be prophesied. For the study of the velocity of blood flow within the animal organism, direct measurements must therefore be restorted to.

THE PRINCIPLE OF THE METHOD UTILIZED: ITS ADVANTAGES AND LIMITATIONS

By the velocity of flow is meant the time required for a certain length of the fluid column to pass a given point, or conversely, how long a certain cross section of fluid takes to flow a definite distance.

The impossibility of securing such information along the brachial and pulmonary vessels during life is evident. However difficult it may be to measure arteriolar and capillary lengths, and the length of venules, one can, nevertheless, accept the fact that from individual to individual, the path traversed by a given particle must be approximately uniform. We have, therefore, as described in a preceding communication, measured the time necessary for the transportation of a minute amount of radium C through an arbitrarily chosen portion of the circulatory system; namely, from the antecubital vein of one arm to the antecubital artery of the other arm. Only the pulmonary capillaries are traversed, and so the variability of the peripheral capillaries is largely, though not entirely, obviated. The time required for the active deposit of radium to flow from the point of injection to the point of detection has been referred to as "the arm to arm circulation time."

In order that changes of the circulation time should be significant, it is of primary importance that under physiological conditions the path travelled should be uniform. That the path traversed is uniform is attested to by a considerable body of evidence. Our own measurements in over one hundred normal persons show agreement within a relatively small range. Repeated tests on the same individual at different times show close correspondence. The work of Hering (1) on horses in 1828, the investigation of Vierordt (2) in 1858

on various small animals, and, more recently, the work of G. N. Stewart (3) on dogs and cats; all these studies strongly support the conclusion that the path traversed is a uniform one.

Although there is general uniformity of the path traversed, it must be recognized that, since one notes the time of the arrival of the first oncoming portion of the active deposit, the circulation time measured represents the velocity flow of the fastest particle through the shortest path. That slight possible variations in the length of the larger vessels might alter the circulation time significantly is opposed by the findings of Hering (1), Vierordt (2), and more recently, Stewart (3). Hering found that the circulation time from the jugular vein of a horse to the tarsal vein required only several seconds more than the circulation time from the jugular vein to the other jugular vein. The possible slight differences in length between the various precapillary or post-capillary vessels involved in the arm to arm pathway in man must therefore produce but an insignificant effect on the circulation time.

One might contend that, although the circulation time would not be seriously affected by variation in the length of arterioles, arteries, venules, or veins, nevertheless it would be appreciably altered by changes in the number of available capillary pathways through the lungs. Unfortunately, the question as to whether there is a significant vasomotor control of the pulmonary circulation is still in dispute. Wiggers (4), in an excellent review of the question, concludes with Schäfer that the fact that "the pulmonary system is provided with vasomotor nerves can no longer admit of doubt", but states that "provided the degree of lung inflation and heart rate remain unaltered, the vessels, that is to say, the arterioles, capillaries, and venules do not show any changes in size, nor is there any evidence of disappearance and reappearance of active capillaries". Wearn, Barr and German (5), on the other hand, by carefully cutting away the chest wall without injuring the parietal pleura of the cat, were able to observe the capillaries of the lungs without in any way manipulating the pulmonary tissue. They found that the capillaries of the lungs exhibited spontaneous variation in calibre.

Certain observations of G. N. Stewart (6), however, offer indirect evidence in this connection. He states (p. 27) "that the observed time of passage of the altered column of blood over an artery, when

salt or pigment solution is infused into the jugular vein, is in general not much longer than the time for which the infusion is kept up". This observation indicates that with animals under the experimental conditions of the study, there existed no partially closed capillaries. For, if such existed, it would follow that they would offer greater resistance to the blood flow than other capillaries more widely open, and that the flow through them would be hindred so as to cause a tailing-out of the altered column of blood. G. N. Stewart's observations would be in accord, however, with a situation in which the capillaries were either widely open or completely contracted.

Our own observations, in the course of measurements in which radium C was used, do not afford additional evidence, because once the time of arrival of radium C is noted, the effect remains continuously present. In general, therefore, it must be stated that experimental evidence is still contradictory concerning the question of the vasomotor control of the pulmonary circulation. It should be emphasized, however, that no matter how the issue may eventually be decided, the constancy of the findings obtained by us in the same persons on different days, indicates that such vasomotor effects, if present, are not of sufficient importance to alter the clinical or physiological significance of our results.

A further objection to the use of the circulation time as an index of the mean velocity of blood flow is to be found in the argument that the method used measures, not the actual velocity, but rather the speed of flow of the more swiftly moving central portion of the blood stream. The argument may seem to contain an element of plausibility, but further analysis of the theoretical and experimental evidence weighs heavily against this possibility. In the first place, fluid flowing through a tube cannot be considered analogous to a piston moving in a cylinder. In the case of a piston, the entire friction occurs between the piston and the cylinder, whereas in a fluid every portion of the fluid develops friction against every other portion of the fluid. When one bears in mind that each smallest portion of the fluid is constantly subject to varying frictional forces, and is, therefore, undergoing corresponding variations in its velocities, and that this situation is altered by discontinuous pulsatile waves with outward expansion and inward vibratory rebound in the case of the arteries, and by variable respira-

tory waves in the case of the veins, and when, furthermore, one considers the innumerable branchings, the impossibility of what is the centrally moving stream at one time remaining the centrally moving stream at all other times, becomes manifest. This question has been fully discussed by G. N. Stewart (6).

Not only theoretical considerations, but practical experience weighs against the velocity of flow of the central stream being far greater than the velocity flow of the outer stream. If the central stream velocity were far greater than the peripheral stream velocity, one would find that, following the injection of dyes into one vein, samples of blood obtained from another would show considerable "stringing out", because the dye carried in the central stream would appear relatively early, and would be followed only later by the dye carried in the more slowly moving peripheral stream. This problem was also carefully studied by G. N. Stewart, who found that such "stringing out" was inconspicuous.

By studying the pulmonary circulation time, the quantity of blood in the lungs, and the output of the heart in one and the same animal, G. N. Stewart was able to secure valuable evidence to show that circulation times determined by the injection method afford a reliable index of the mean velocity.

"If V is the minute volume of the heart in cubic centimeters, T, the mean circulation time of the lungs or of the lesser circulation in seconds, and Q the average quantity of blood in the lungs in cubic centimeters, or in the lesser circulation at the time when V and T are measured; then $V = \frac{Q\,60}{T}$. Even if some deduction is made from V for possible overestimation of that quantity, Q still comes out so high that it is not possible to assume, as Tigerstedt has done, that methods depending on injection of salts or pigments into the circulation give much too low a value for T, owing to the 'hastening on' of a portion of the injected substance in the axial stream. In a network of capillaries filled with blood corpuscles, it is not conceivable that the same particle of injected material should continue moving with the maximum velocity for more than a small fraction of the total circulation time, its path being necessarily an 'out and in' one. If we were to increase T materially above the actually observed (corrected) time, Q would come out impossibly high."

Although, in our experience, considerable "stringing out" occurs in pathological conditions of the circulation, one cannot interpret this

as necessarily a result of the different velocities of the central and peripheral streams. In measurements of the velocity of blood flow in patients with congestive failure, we found that the concentration of the first portion of the radioactive substance to arrive in the antecubital artery was considerably less than the concentration of radium active deposit in the first oncoming portion in normal persons. The concentration of the radium C increased moreover relatively slowly after its initial appearance. It was, therefore, necessary to increase slightly the amount of active deposit of radium injected. In order to be certain that the first diluted portion of the oncoming head of active deposit had not escaped detection, we performed check measurements both by means of our own procedure and by means of the injection of fluorescein. These results showed that the radium active deposit is detected in the arterial vessels about the elbow in patients with cardiovascular disease as it is in normal persons. The common clinical observation that the signs of congestion of the pulmonary circulation appear first at the bases of the lungs suggests that the "stringing out" effect observed in circulatory insufficiency may well be due to the fact that some of the blood flows rapidly through the upper, relatively normal, portions of the lungs, whereas other portions of the radium C which appear later are carried by the blood through other, more congested portions. Drinker, Churchill and Ferry (7), in a recent study of the volume of blood in the heart and lungs, observed a similar condition. They state

"One may assume that under rapid rates of blood flow all of the pulmonary capillaries are conducting blood and that the rate of movement in individual capillaries approaches equality, but that as blood flow into the right ventricle falls off, the easiest routes are chosen, and with exceedingly low blood flow, many capillaries contain blood which is practically not in motion or which is moved slowly into the pulmonary veins."

Another source of variation in the circulatory system which might lead to slight differences in the circulation time has been noted by several observers, and was first discussed by Vierordt (2). He states

"If the first portion of the solution reaches the right auricle towards the end of diastole, it will meet blood which has flowed from the place of injection to the heart before the injection was made. The next ventricular systole therefore dis-

charges the blood containing the solution as well as the blood that has flowed just previous to the injection, and so the circulation time may be shortened by almost as much as the time required for a single systole. A similar situation may arise in the left heart. The error will obviously be greater (*1*) when the first portion of the injection mass arrives in the auricle shortly before its next systole. If this portion is small, then through dilution, it will not be detectible; if, however, it is larger it will make itself manifest. (*2*) The more incompletely the chambers contract, and (*3*) the slower the heart rate . . . . the greater will the error tend to be."

But even with the ventricular rate as low as sixty per minute the error must be less than two seconds.

Finally we wish to point out that, whatever objections may be made to the use of the circulation time as a measure of the mean velocity of blood flow, these objections cannot impair the clinical significance of such observations for comparative purposes.

THE RELATION BETWEEN THE ARM-TO-ARM CIRCULATION TIME, THE VITAL CAPACITY AND THE VENOUS PRESSURE

Examination of the results of our studies on the relation of the clinical observations to the measurements of the dynamic aspects of the circulation in patients with cardiovascular disease shows that while the rise of pressure in the antecubital vein measured according to the method of Moritz and Tabora is proportional to the degree of congestive failure, the rise above the upper limit of normal does not occur until relatively late in the decompensatory process. Excluding all possible local causes, we have found that the rise in venous pressure is preceded by a definite period when the vital capacity is reduced and the velocity of blood flow is lessened. A study of the anatomical and physiological characteristics of the veins affords an explanation of this finding.

The muscular elements in veins are few, and elastic fibres are scanty, so that the veins may be considered as easily collapsible, but inelastic tubes. They are freely distensible, therefore, until the limits of their capacities are reached, but only when this limit is reached are they resistant to further stretching. During the stage of increasing venous filling, added amounts of blood result in very small increases in pressure. Once, however, the vessels are full of blood to the limits of

their capacities, these relatively inelastic tubes can expand no further, and any additional amounts of blood flowing into the veins will then result in a conspicuous rise in pressure. This is graphically illustrated by figure 1.

These facts, therefore, indicate that a stage of engorgement precedes an increase of pressure in the veins and only after the veins have become filled to the limits of capacity do additional amounts of blood cause a rise in pressure. In normal resting persons the veins are not filled to their full capacity, and so they are partially collapsed. Their cross sectional area is smaller than when they are fully distended.

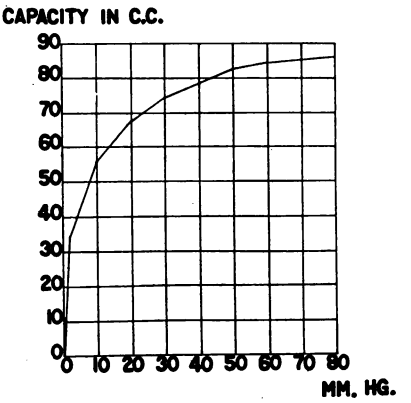

FIG. 1. Curve of distensibility of a vein (by E. H. Starling from figures given by Roy).

Since the velocity of flow is inversely proportional to the cross sectional area, a slowing of the velocity of blood flow would occur provided that the increase in the cross section of the blood stream were not counterbalanced by an increase in the pressure gradient within the veins. Starling showed that the latter possibility is unlikely and our own results are also opposed to such a consideration. The slowing of the blood flow in the veins during the period of increased venous engorgement might therefore be expected to precede, as in fact it does precede, the occurrence of increased venous pressure. In all probability, similar events occur in the lungs and explain why the reduction in the velocity of blood flow occurs so early in circulatory failure. That the

engorgement of the lungs leads to a diminution in their elasticity and so causes a limitation of the normal movements and a reduced vital capacity, has been suggested by previous observers (Von Basch, Siebeck, Peabody). With engorgement and distention of the pulmonary vessels, increase in the total cross sectional area of the blood stream through the lungs may well occur and lead to reduction in the velocity of blood flow.

Consideration of the relation of filling to pressure and elasticity of the blood vessels suggests that this is at least one factor why the rise in peripheral venous pressure and appearance of edema in the lungs, are preceded by definite retardation in the velocity of blood flow, and by reduction in the vital capacity. The question still remains, however, as to whether beginning congestive failure is signalled first by lessened velocity of blood flow, or by reduction in the vital capacity. Although the sequence of events was not uniform in all types of cardiovascular disease, it may nevertheless be stated that the vital capacity was generally reduced first.

Several explanations of this finding suggest themselves. It is conceivable that the underlying, and as yet by no means clearly understood, mechanisms which are responsible for the lowered vital capacity may precede the mechanisms responsible for the slowing of the blood stream through the lungs. Another possibility must be recognized, however. The arm-to-arm circulation time, as tested by our method, measures the time required for the fastest particle of radioactive substance to travel from the point of injection in the antecubital vein to the opposite brachial artery. The circulation time is therefore a somewhat simple expression of the blood flow in the arm as well as the blood flow in the lungs. That the blood flow in the arms is extremely variable has been shown by previous observers (G. N. Stewart (8), Hewlett and Van Zwalwenburg (9)), and it is possible that these relatively great variations of blood flow in the arm may obscure variations of the blood flow in the lungs, which, while small, may nevertheless be an early and important indication of the beginning of circulatory failure. Measurements of the pulmonary circulation time and of the pulmonary minute volume flow in man would be of considerable interest in this connection. A third possible explanation exists and should be stated. Clinical evidence, such as the appearance of moist râles first at the bases of the lungs, supports the possibility that passive congestion

may occur earliest, and perhaps exclusively, at the bases of the lungs. If it appears while the circulation through the upper portions of the lungs is still normal, a reduced vital capacity may exist in the presence of normal pulmonary circulation time.

Which of these possibilities is the true one cannot be established on the basis of the evidence now available, but studies are in progress to clarify the problem.

SUMMARY

1. Evidence is presented that the arm-to-arm circulation time in normal resting individuals is a measure of the mean velocity of blood flow.

2. Our clinical measurements and the experimental evidence of others indicate that the path traversed by the radium C is uniform from patient to patient.

3. With the onset of circulatory insufficiency, the vital capacity shows a decrease somewhat earlier than the velocity of blood flow; whereas the rise in venous pressure occurs only when the circulatory failure is considerably more pronounced.

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