STUDIES ON THE VELOCITY OF BLOOD FLOW: *VII. The Pulmonary Circulation Time in Normal Resting Individuals*

Herrmann L. Blumgart, Soma Weiss

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STUDIES ON THE VELOCITY OF BLOOD FLOW

VII. The Pulmonary Circulation Time in Normal Resting Individuals[1]

By HERRMANN L. BLUMGART and SOMA WEISS

(From the Thorndike Memorial Laboratory, Boston City Hospital and the Department of Medicine, Harvard Medical School)

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This paper presents the first measurements of the velocity of blood flow through the lungs of man. Thorough understanding of the blood flow through the lungs is of great significance in understanding adaptations of the circulation in health and disease.

The study of the pulmonary circulation has, therefore, always attracted the interest of investigators. The literature is voluminous and was reviewed in 1903 by Tigerstedt (1) and in 1921 by Wiggers (2).

In animals the study of the pulmonary circulation necessitates such distortion of the normal physiological conditions that interpretation of the results is difficult. The chest has usually been opened, the negative intrathoracic pressure abolished, and normal inspiration has been replaced by forcible distention of the lungs with positive blasts of air. By such methods Plumier (3) in 1904 first studied the pulmonary circulation time in animals, estimating the time between release of a previously compressed vena cava and the subsequent maximal rise in arterial pressure. G. N. Stewart (4) (19) advanced the knowledge of the pulmonary blood flow by studying the time required for dyes and salt solutions to pass from the great veins through the heart and lungs to the great arteries. The chest was not opened although the animals were under general anesthesia. His results will be discussed later.

Because such experiments are clinically not feasible, and because

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the results of investigations on animals can be translated into terms of human physiology only with difficulty, the study of the pulmonary circulation in man has been pursued along somewhat different paths. The most trustworthy information has been elicited by studying the pulmonary minute volume flow by the principle of Fick. Although exceedingly important information has been obtained, the usefulness of the procedure has been limited because of certain inherent difficulties. The analysis of air and blood samples is complicated, and collection of air samples demands intelligent coöperation on the part of the subject. The clinical usefulness of the procedure has also been restricted because the method is inapplicable in the presence of profound circulatory disturbance associated with dyspnea. To quote recent investigators, "the existing methods applicable to human subjects require intelligent coöperation and they are at best tedious and subject to error'' (5). In short, the existing methods for studying the pulmonary minute volume flow are inadequate and no method for measuring the velocity of blood flow through the lungs in man is available.

Previous studies (6, 7, 8, 9, 10, 11) have shown that the arm to arm circulation time can be measured in man by injecting the active deposit of radium into the antecubital vein of one arm and subsequently, by means of a suitable detecting device, noting its time of arrival in the arteries about the elbow of the other arm. It seemed that if the procedure for measuring the arm to arm circulation time could be adapted to the measurement of the pulmonary circulation time in man, the information obtained would be valuable for the following reasons. 1. Information would be secured about a fundamental aspect of the pulmonary circulation hitherto unstudied in man. 2. The pulmonary circulation could be studied under both normal and pathological conditions without in any way interfering with the phenomena under observation. 3. The method would be quantitative, objective, and require no coöperation from the patient. 4. The effect of the variability of the peripheral capillary circulation would be obviated. Previous investigators as, for example, G. N. Stewart (12), and Hewlett and Van Zuwaluenburg (13) found considerable variations in the volume flow of the arm which bore no constant relation to general bodily conditions.

Since the circulation of blood through the lungs has considerable physiological and clinical significance, it seemed desirable to measure the velocity of blood flow through the lungs complicated as little as possible by extraneous factors. Small changes might be of considerable significance and still be entirely obscured by relatively large fluctuations in the arm blood flow. After considerable experimentation, the following procedure has been found most satisfactory in the the study of the velocity of blood flow through the lungs.

METHOD

The principle of the method. The method is a further development of the procedure devised for the study of the arm to arm circulation time. The active deposit of radium, that is to say, radium C, is injected into the antecubital vein of one arm and its time of arrival is observed first, in the right chambers of the heart, and later in the arteries about the elbow of the other arm. As mentioned in previous studies, active deposit of radium is particularly suited to the purpose. Of primary importance is its non-toxicity in amounts used. Quick and Duffy (14) at the Memorial Hospital in New York, in studying the possible therapeutic effects of radium C in patients with advanced generalized carcinomatosis, repeatedly gave intravenous injections of 50 and 75 millicuries, amounts five to eight times those used by us, without any consequent ill effects. They studied the urine for signs of renal irritation and the blood for evidence of nitrogen retention without noting any untoward reactions. No significant changes occurred in the red cell count or hemoglobin.

The injection of radium C by us into animals, and later into ourselves and other normal subjects has shown a uniform absence of any objective or subjective ill effects over a period of time in which four hundred and fifty measurements of the velocity of blood flow have been made. In a few instances, short temporary thrombosis of the injected vein occurred without causing any ill effects to the patients. The incidence of thrombosis in our experience was no higher than that occurring with other diagnostic procedures. In the first one hundred and fifty patients the urine was examined before and after the observation, and in no instance were any signs of the slightest renal irritation disconcernible, nor were any changes in the blood noted. None

of the patients has shown any delayed reaction. This is of particular interest in connection with ourselves, for not only have we measured our blood flow by injecting active deposit of radium, but we have been exposed to the beta and gamma radiation of the active deposit used in all the observations. Hence, through such cumulative effects, any untoward reaction would become manifest earlier in us than in patients.

The absence of any demonstrable biological effects of radium C in the course of our investigations is in no way surprising for the amounts necessary for a measurement of the velocity of blood flow is but 1 to 10 millicuries of active deposit of radium. Such an amount is infinitesimal and corresponds in weight to 10^{-15} grams. It should

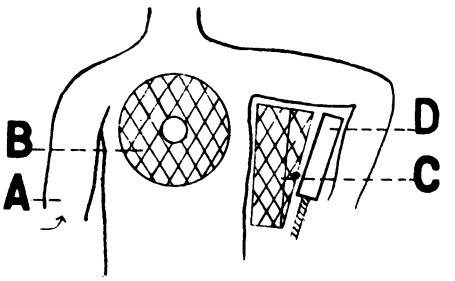

FIG. 1. RELATION OF PATIENT TO DETECTORS AND LEAD SHIELDS

be noted that millicuries of active deposit do not correspond in weight to radium itself for a millicurie of active deposit signifies the amount which is *in equilibrium* with a millicurie of radium emanation. A millicurie of emanation, in turn, is that amount which is *in equilibrium* with a milligram of radium element.

The character of the radiation of active deposit is peculiarly suited to velocity of blood flow measurements. Of the three types of radiation emitted by radioactive substances, the so-called "alpha radiation" is most likely to cause possible toxic effects. Within twenty minutes after the active deposit has been removed from the emanation, the alpha radiation decays to 4 per cent of its initial value. The rapid spontaneous decay of active deposit to a practically inert form, radium D, prevents prolonged exposure of a person to the radiation. Active deposit decreases to 3 per cent of its initial activity within

three hours. Less than the theoretical 3 per cent is present in the body at the end of three hours, however, for a considerable portion of the injected amount is excreted into the intestines and into the urine. Consequently, repetition of the test after three hours is feasible.

In the studies of the velocity of blood flow, active deposit of radium has been used because of its penetrating radiation, which consists of beta particles (or electrons), and gamma rays which are comparable to hard x-rays. These radiations can penetrate ordinary material such as tissues or air, but are absorbed by lead. If, therefore (see fig. 1), the active deposit of radium is injected into the vein of one arm at *A*, the active deposit gives off radiations as it is carried up the arm to the right chambers of the heart. But the lead shield *B* prevents the radiation from reaching the detecting device which has been inserted within the centrally situated hole. This hole is placed immediately over the right auricle (over the sternum in the third intercostal space) so that, upon the arrival of the active deposit within that chamber, the radiations are no longer separated from the detector by lead. Instead, the radiations emerge through the tissues, traverse the air, enter the detecting device and there set up a train of events, finally producing automatic registration of the time of arrival of the active deposit within the right chamber of the heart.

Similarly the radiation from the active deposit as it is carried through the lungs is prevented from reaching the detector *D* by the intervening lead shield *C*. Once the active deposit reaches the arterial vessels immediately in front of the detector *D*, the radiations set up a chain of events similar to that already described by which their time of arrival is automatically registered. The time that elapses between the injection of the active deposit into the antecubital vein at *A*, and the arrival of the active deposit in the right chambers of the heart may be called "the venous velocity time" for it is a measure of the velocity of the venous blood of the arm to the heart. The time that elapses between the arrival of the active deposit of radium in the right chambers of the heart and its arrival in the arteries about the elbow of the arm may be called the "crude pulmonary circulation time." The latter includes, besides the actual pulmonary circulation time, the time spent in passing through the four cardiac chambers and the time necessary for the active deposit to travel through the large arterial trunks

to the place of detection in the antecubital arteries. For reasons which will subsequently be given, the time spent in the heart is approximately one second and the time necessary for the active deposit to travel from the heart to the antecubital arteries is approximately three and three-tenths seconds. Consequently if four and three-tenths seconds are subtracted from "the crude pulmonary circulation time" one obtains an estimate of "the actual pulmonary circulation time".

Originally it was hoped that by placing a detecting device immediately above the heart, as indicated in figure 1, the arrival of the active deposit could be ascertained, and that with the passage of the active deposit into the vessels of the lungs, the ionization effect would diminish only to increase when the active deposit of radium was concentrated again within the left chambers of the heart. Unfortunately, once the ionization effect is observed in the detector placed over the heart, the effect remains persistently present. Further efforts will be made, however, to measure the time of appearance and diappearance of the active deposit in the left chambers of the heart.

Description of the apparatus. The results of the present investigation are based on the detection of the time of arrival of the active deposit in the right chambers of the heart of man and in the arteries about the elbow of the left arm. Instead of the modified C. T. R. Wilson cloud chambers used in the previous "arm to arm circulation time" studies, a smaller detecting device has been utilized. This detecting device which was built and generously loaned to us for our particular purpose by the General Electric Company of Schenectady, New York, is described elsewhere by C. W. Hewlett (15) (fig. 2). In principle this device depends upon the fact that radiations of radium C cause ionization by collision in any gas subjected to high potential differences. *M* (fig. 2) represents a small brass cylinder with a thin aluminum leaf window *A* at one end. *N* is a plug of hard rubber which holds the axially situated platinum electrode *L* in position. *M* is charged to 1200–2000 volts, depending upon the point of the platinum electrode. In the absence of any radioactive substance the air gap serves to insulate the platinum needle at −4.5 volts from the walls of the brass chamber at 1500 volts. A single electron or gamma ray may produce sufficient ionization by collision to cause a slight diminution in the voltage on the needle. This fall of potential is converted

into current flow by a three electrode vacuum tube. In the plate circuit of this tube is a recording pen galvanometer manufactured by Mr. A. A. Clokey of Rutherford, New Jersey. Attached to the moving coil Y (fig. 2) of the galvanometer CXY (fig. 2) is a light glass capillary which records any movements of the galvanometer on a moving paper

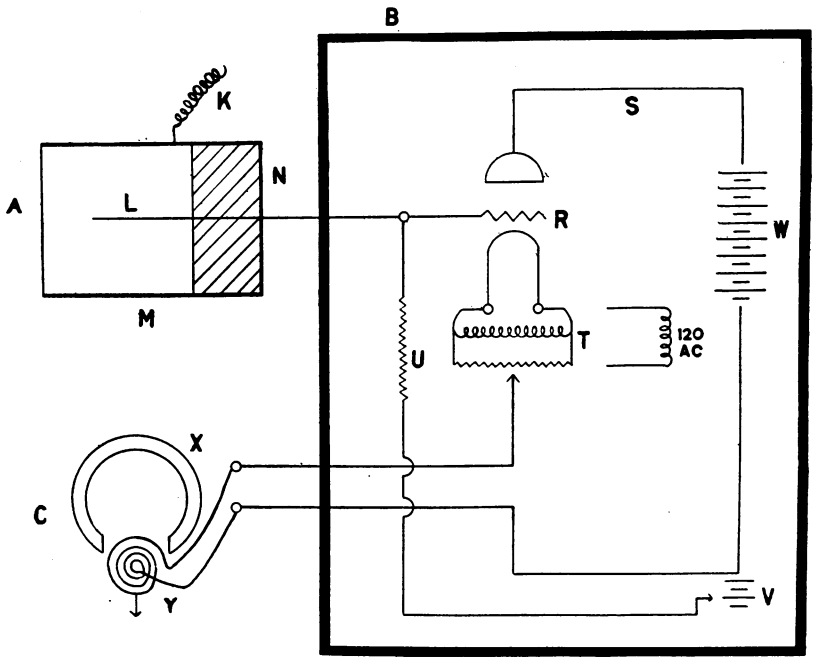

FIG. 2. DIAGRAM OF DETECTOR AND RECORDING SYSTEM

M indicates brass cylinder; *A*, thin aluminum window; *K*, lead for high voltage; *N*, hard rubber plug; *L*, platinum needle; *B*, amplifying unit consisting of *R*, three electrode vacuum tube; *T*, transformer for filament of tube; *S*, plate of tube; *W*, plate batteries, *V*, batteries for bias for high grid resistance *U*, and *XYC* recording pen galvanometer.

tape. The appearance of radium C beneath the detector instantly produces a train of events which terminates in the automatic inscription by a pen and ink record on a moving paper tape. By means of a signal magnet and time clock the time is also recorded in seconds.

The lead shields *B*, and *C* (fig. 1) are designed to absorb the

maximal percentage of radiation. Shield *B* is 22 cm. in diameter and 17 cm. in height. The diameter of the centrally bored hole is 4 cm. The ionization chamber is placed within the block with its window or lower end 10 cm. from the bottom of the block. The lead block *C* consists of several separate parts designed to utilize the available space between the arm and the thorax. The position of the lead block can be adjusted by means of a hydraulic pump device, which was built and generously loaned to us by the General Electric Company, Schenectady, New York.

Critique of method. To observe whether the active deposit of radium produces ionization in the detector before it arrives in the right chambers of the heart would theoretically demand continuous withdrawal of blood from the right auricle and of making tests for the presence of radium C simultaneously with the inscription of the record. Obviously this is not feasible. Instead, with the apparatus arranged precisely as in the actual velocity tests, active deposit of radium equivalent or greater than the amount usually injected was brought gradually toward the hole in the lead block along a path similar to that traveled within the veins leading to the right chambers of the heart. Many observations have uniformly demonstrated the fact that the appearance of the active deposit beneath the hole is signalled immediately by a continuous ionization effect of such increased magnitude as to leave no doubt as to the precise position of the source of the radiation.

The same considerations discussed in a previous paper (7) regarding the critique of the method apply to the measurement of the time of arrival of the active deposit in the antecubital arteries of the arm and will not be repeated. The method of detection is exactly similar except that a small ionization chamber is used instead of the more cumbersome modified C. T. R. Wilson cloud chamber. The sensitivity of both detectors is identical and results obtained by one device are in complete accord with those gained by means of the other.

Procedure of the measurement of the pulmonary circulation time. The preparation of the active deposit and the technique of its intravenous adminstration is described in a previous communication. Measurement of the velocity of blood flow is made under basal metabolic conditions, no food being taken by the patient after supper of the

preceding evening. The person lies at rest in bed at least twenty minutes before the test. The site of arterial pulsation of the brachial artery is marked with ink and the left arm is passed around the lead blocks so that the window of the detector is just in front of the line of maximum arterial pulsation. The position of the right auricle is indicated by a circle of ink painted on the skin of the chest over the sternum between the third and fourth ribs. The patient is placed with the spot of ink immediately beneath the hole in the lead block (fig. 1), *B*. The ionization chamber with its cable leading to the amplifier and recording systems is then inserted into the hole of the lead shield. The active deposit, the volume of which does not exceed 0.2 cc., is not injected for at least twenty minutes after it has been removed from the

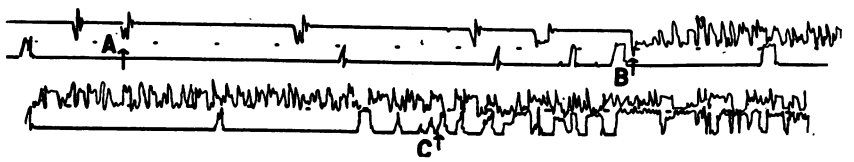

FIG. 3. RECORD OF PULMONARY CIRCULATION TIME MEASUREMENT

Middle dots signify time in seconds. Upper line is the tracing made by the recording pen of the detector over the right auricle; lower line, similar record of the detector placed against the brachial artery. *A* indicates the instant of injection into right antecubital vein; *B*, the time of arrival of active deposit into right auricle; *C*, the time of arrival of active deposit in the left antecubital arteries.

radium emanation in order to allow a decrease of alpha ray activity to 4 per cent. The precautions previously described are observed in carrying out the intravenous injection (7, 11).

As the active deposit is carried in the blood stream to the right chambers of the heart, an occasional deflection of the galvanometer recorder of the heart detector can be seen. With the arrival of the active deposit in the right chambers of the heart, the emergent beta particles and gamma rays pass through the tissues of the chest, traverse the air, and entering through the thin window of the ionization chamber, set up a continuous disturbance in a siphon feed recording pen of the galvanometer which registers in ink on a moving tape. The occasional deflections occurring before the continuous activity of the galvanometer are due to the occasional gamma rays which penetrate

the lead block. Elimination of these occasional deflections would require a lead block of undue proportions. The arrival of the radium active deposit in front of the detecting device is accompanied by an ionization change of such magnitude as to leave no doubt of its time of arrival (fig. 3). The time between the intravenous injection and the arrival of the substance in the right heart represents the velocity of blood flow between the two points. As the active deposit travels through the body, an occasional disturbance occurs in the detector placed against the artery of the arm. With the arrival of the active deposit within the arterial vessels about the elbow, emergent beta particles and gamma rays pass into the ionization chamber and produce a continuous disturbance which is registered on the same tape by a second siphon feed recording pen galvanometer. The time is marked in seconds by an electromagnetic timer. The time of injection may be automatically recorded by the device described in a previous communication (11). Consequently the paper tape serves for the automatic registration of all the data.

All the persons in whom the velocity of pulmonary blood flow was measured were either healthy or convalescent from some disease which was neither cardio-respiratory, metabolic, or haemic in nature. Many of the patients were from the surgical services and were ready to be discharged from the hospital. Physical examination revealed no cardio-respiratory abnormalities. The temperature, the pulse and the respiration were noted. The pulse was again counted immediately upon the completion of the observation. The age was recorded and the weight, height and arterial blood pressure measured. The venous pressure was estimated by the direct method of Moritz and Tabora (16), just before the active deposit of radium was injected. The vital capacity was taken immediately on the completion of the measurement of the velocity of blood flow. The results of our observations are tabulated below (table 1).

Figure 4 graphically presents the incidence of the variations in the velocity of the venous blood from the arm to the heart and figure 5 in similar manner presents the data in regard to the crude pulmonary circulation time. Comparison of these two diagrams indicates that the fluctuations in the pulmonary circulation times are less than that of the venous velocity time.

TABLE 1

Duplicate measurements of the pulmonary circulation time in the same person

Number of measurements	Date	Name	Age	Surface area	Pulse rate	Vital capacity	Vital capacity per square meter	Arterial pressure		*Venous pressure H_2O	Circulation time			Circulation time per square meter		
								Systolic	Diastolic		Arm to heart	Arm to arm	Pulmonary	Arm to heart	Arm to arm	Pulmonary
				square meter		*cc.*	*cc.*	*mm.*	*mm.*	*cm.*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*
275	October 26, 1926	C. W.	17	1.60	105	3,700	2,312	126	64	+3.0	5.5	12.5	7.0	3.4	7.8	4.3
310	November 19, 1926	C. W.	17	1.60	93	4,300	2,690	114	54	−1.0	5.5	13.0	7.5	3.4	8.1	4.7
311	November 19, 1926	M. A.	23	1.67	77	Patient unable		124	58	+16.0	11.5	20.0	8.5	6.9	11.9	5.0
314	November 23, 1926	M. A.	23	1.67	85	to coöperate		124	76	+11.0	5.5	16.5	11.0	3.3	9.8	6.5
373	February 18, 1927	J. S.	23	1.74	83	4,400	2,525	126	72	+8.0	9.0	19.0	10.0	5.1	10.9	5.2
374	February 18, 1927	J. S.	23	1.74	96	4,400	2,525	126	72	+6.5	11.5	18.0	6.5	6.6	10.3	3.7
375	February 23, 1927	J. M.	21	1.84	69	4,900	2,662	110	76	−1.5	7.0	21.5	14.5	3.8	11.6	7.8
378	February 23, 1927	J. M.	21	1.84	66	4,900	2,662	110	76	−1.0	8.0	19.0	11.0	4.3	10.3	5.9
382	February 26, 1927	P. M.	21	1.57	67	4,100	2,611	126	64	−1.0	4.5	15.5	11.0	2.8	9.8	7.0
383	February 26, 1927	P. M.	21	1.57	76	4,100	2,611	126	64	−0.5	6.5	18.5	12.0	4.1	11.7	7.6
390	March 16, 1927	A. W.	22	1.66	60	4,200	2,529	106	68	+18.0	14.0	26.0	12.0	8.4	15.6	7.2
392	March 16, 1927	A. W.	22	1.66	63	4,200	2,529	106	68	+6.5	6.5	20.5	14.0	3.9	12.3	8.4
400	March 21, 1927	H. B.	36	1.51	78	2,900	1,921	112	60	−2.0	7.0	20.0	13.0	4.6	13.2	8.6
402	March 21, 1927	H. B.	36	1.51	80	2,900	1,921	112	60	−1.5	6.0	21.0	15.0	3.9	13.9	9.9
286	October 28, 1926	G. Y.	24	1.74	98	Unable to ob-		174	84	+13.0	3.5	10.0	6.5	2.0	5.7	3.7
413	April 21, 1927	G. Y.	24	1.74	98	tain		128	76	+11.5	7.0	13.5	6.5	4.0	7.7	3.7

* To conform to the level of the right auricle, 5.0 cm. should be added to these figures.

In order to learn what variations may occur in a given individual repeated measurements were performed under conditions as similar as possible. The results are presented in table 1. The maximum variation was three and a half seconds and the average in eight persons was two seconds. Table 2 presents our findings in sixty-two tests. The data include measurements of the pulmonary circulation time, the venous velocity time, the vital capacity, and the arterial and

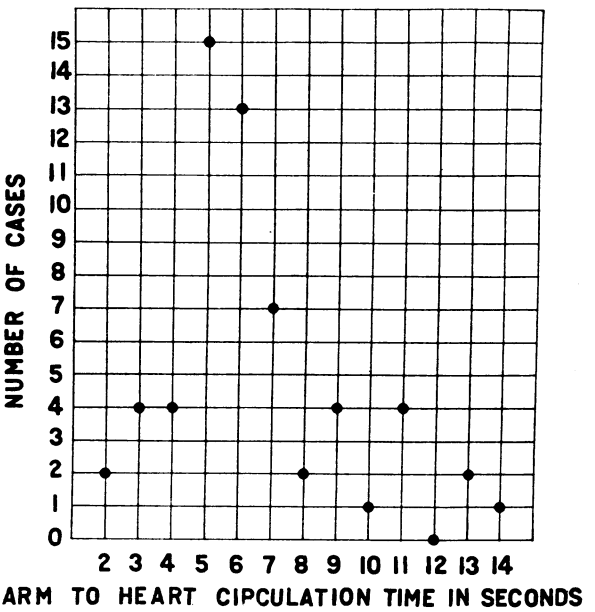

FIG. 4. THE VELOCITY OF VENOUS BLOOD FROM THE ARM TO THE HEART—IN 62 CASES

venous pressures. The venous velocity time varied from two to fourteen seconds. The average venous velocity time in fifty-nine measurements was seven (6.7) seconds; the pulmonary velocity time varied from five to seventeen; the average crude pulmonary circulation time (sixty-two measurements) was eleven (10.8) seconds.

In certain individuals, the pulmonary circulation time was longer than seventeen seconds. This was accompanied at times by a prolongation in the venous velocity time and was not infrequently asso-

ciated with an unduly high venous pressure. Some of these persons had definite stigmata of psychoneurosis. Whether this phenomenon is due to the abnormal behavior of the peripheral vasomotor system as evidenced by the cold cyanotic hands of these patients, or whether the delay may be due to other factors is not as yet determined.

Discussion of the method. The time elapsing between the arrival of the actve deposit of radium in the right chambers of the heart and its arrival in the arteries about the elbow of the arm may be termed "the crude pulmonary circulation time". The average in sixty-

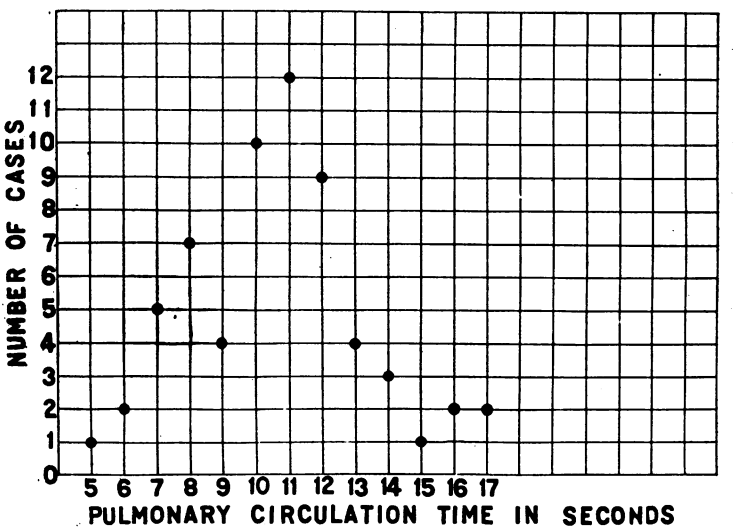

FIG. 5. PULMONARY CIRCULATION TIME (CRUDE) IN SECONDS—62 CASES

two measurements was 10.8 seconds. This time includes, in addition to the actual pulmonary circulation time, the time of transit through the chambers of the heart and the time taken by the active deposit in traveling from the heart to the antecubital arteries. The velocity of arterial blood flow is conspicuously rapid, particularly in vessels as large as the aorta, the subclavian and brachial arteries. We have not as yet, by means of the radium active deposit method, actually measured the veolcity of blood flow in arteries. Hermann (17) inferred from anatomical and physiological data that the velocity

TABLE 2

Measurements of the pulmonary circulation time and related aspects in normal resting male individuals

Number of measurements	Date	Name	Age	Surface area	Pulse rate	Vital capacity	Vital capacity per square meter	Arterial pressure		*Venous pressure H_2O	Circulation time			Circulation time per square meter		
								Systolic	Diastolic		Arm to heart	Arm to arm	Pulmonary	Arm to heart	Arm to arm	Pulmonary
	1926			*square meter*		*cc.*	*cc.*	*mm.*	*mm.*	*cm.*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*
245	September 24	P. S.	19	1.68	75	3,250	1,934	130	85	+2.0	6.0	16.0	10.0	3.5	9.5	5.9
250	September 28	Jo. D.	22	1.64	62	3,900	2,378	140	70	+1.0	7.0	20.0	13.0	4.2	12.1	7.9
253	September 28	G. B.	25	1.78	69	4,250	2,387	115	80	−2.0	4.75	15.0	10.0	2.8	8.4	5.6
											2.0		10.0	1.1		5.6
254	September 28	I. B.	21	1.78	74	4,600	2,584	104	65	−1.5	3.0	12.0	9.0	1.6	6.7	5.0
								164	90							
255	September 28	V. F.	19	1.66	86	4,150	2,500	166	94	0.0	3.5	12.0	8.75	2.1	7.2	5.1
											4.0		11.0	2.3		6.5
256	September 30	E. A.	23	1.67	97	4,500	2,814	124	94	+1.5	3.0	15.0	12.0	1.7	8.9	7.1
260	September 30	J. D.	26	1.55	94	3,700	2,387	120	80	−2.0	7.0	16.0	9.0	4.5	10.3	5.8
262	September 30	W. C.	21	1.99	75	4,700	2,361	114	58		7.5	15.0	8.5	3.7	7.5	4.0
263	October 19	J. S.	17	1.77	102	3,800	2,146	125	70	+2.0	5.0	15.0	10.0	2.8	8.4	5.6
266	October 19	J. P.	49	1.55	52	4,100	2,645	125	55	+3.0	5.0	18.0	13.0	3.2	11.6	8.3
269	October 21	F. B.	24	1.72	86	4,100	2,383	112	74	−1.5	5.5	17.0	11.5	3.1	9.8	6.6
273	October 21	J. K.	30	1.86	75			118	64	−1.0	6.0	18.0	12.0	3.2	9.6	6.3
274	October 21	R. B.	20	1.84	80	4,500	2,445	118	76	+1.0	5.0	16.0	11.0	2.7	8.6	5.9
275	October 26	C. W.	17	1.60	105	3,700	2,312	126	64	+3.0	5.5	12.5	7.0	3.4	7.8	4.3
277	October 26	R. P.	55	1.71	84	4,250	2,485	112	66		8.0	17.0	9.0	4.6	9.9	5.2
279	October 26	W. V.	17	1.68	94			98	56	+2.5	3.5	10.5	7.0	2.0	6.2	4.1

280	October 26	A. M.	38	1.57	69	3,700	2,356	78	54	−1.5	7.0	17.0	10.0	4.4	10.8	6.3
281	October 26	T. C.	64	1.97	74	3,600	1,872	132	74	−2.0	4.0	14.0	10.0	2.0	7.1	5.0
285	October 28	J. W.	48	1.86	70	4,200	2,257	120	62		4.0	17.0	13.0	2.1	9.1	6.9
286	October 28	G. Y.	24	1.74	98			174	84	+1.3	3.5	10.0	6.5	2.0	5.7	3.7
288	October 28	A. G.	52	1.55	68	5,500	2,258	120	72	+2.0	6.0	16.5	10.5	3.8	10.6	6.7
289	October 28	J. B.	43	1.81	92	4,500	2,486	116	62	−1.0	6.0	13.5	7.5	3.3	7.4	4.1
291	October 28	A. M.	38	1.57	72	3,700	2,356	76	50				17.0			10.8
297	November 4	E. D.	62	1.67	62	4,000	2,397	106			6.5	15.5	9.0	3.8	9.2	5.3
299	November 4	T. F.	65		72			132	76	−3.0	5.5	13.0	7.5			
310	November 19	C. W.	17	1.60	94	4,300	2,690	114	54	−1.0	5.5	13.0	7.5	3.4	8.1	4.7
311	November 19	M. A.	23	1.67	76			120	60	+1.6	11.5	20.0	8.5	6.9	11.9	5.0
313	November 23	A. J. G.	52	1.54	92	3,200	2,129	118	62	+5.5	13.0	25.0	12.0	8.4	16.2	7.8
314	November 23	M. A.	23	1.67	88			124	76	+19.5	5.5	16.5	11.0	3.3	9.8	6.5
317	November 23	E. J.	24	2.00	100	5,900	2,950	92	70	−1.0	9.0	17.0	8.0	4.5	8.5	4.0
320	November 23	P. S.	65	1.63	66			126	76	−3.0	6.5	18.0	11.5	3.9	11.0	7.0
328	December 14	W. G.	43	1.83	74	4,200	2,295	116	66	+12.0	5.0	17.0	12.0	2.7	9.3	6.7
329	December 14	J. B.	26	1.71	88	3,800	2,221	118	80	+1.5	6.5	16.5	10.0	3.8	9.7	5.9
	1927															
343	January 18	J. C.	35	1.59	83	3,100	1,950	106	66	+8.5	5.0	13.0	8.0	3.1	8.1	5.0
344	January 18	E. F.	24	1.79	54	4,100	2,290	108	64	+4.0	5.5	16.5	11.0	3.0	9.2	6.1
348	January 19	C. W.	35	1.74	112	4,000	2,300	120	58	+8.5	6.0	14.5	8.5	3.4	8.3	4.8
349	January 19	W. H.	35	1.72	103	5,150	2,995	114	64	+4.5	5.5	13.5	8.0	3.1	7.8	4.6
350	January 19	M. M.	35	1.68	111	3,950	2,352	108	70	+6.5	5.0	15.0	10.0	2.9	8.9	5.9
351	January 18	J. D.	24	1.86	79	4,500	2,419	118	64	+1.5	7.5	19.0	11.5	4.0	10.2	6.1
356	February 9	F. A.	36	1.66	87	3,250	1,957	102	66	−2.0	5.0	21.0	16.0	3.0	12.6	9.6
364	February 14	J. M.	21	1.85	94	5,050	2,729	112	80	−1.5	4.0	16.0	12.0	2.1	8.6	6.4
366	February 15	C. C.	29	1.70	57	4,500	2,648	106	60	+4.5	10.5	22.0	11.5	6.1	12.9	6.7
367	February 16	C. G.	25	1.84	50	5,000	2,719	106	66	−1.0	6.5	18.0	11.5	3.5	9.7	6.2
373	February 18	J. S.	23	1.74	83	4,400	2,527	126	72	+8.0	9.0	19.0	10.0	5.1	10.9	5.2
374	February 18	J. S.	23	1.74	96	4,400	2,527	126	72	+6.5	11.5	18.0	6.5	6.6	10.3	3.7
375	February 23	J. M.	21	1.84	69	4,900	2,662	110	76	−1.5	7.0	21.5	14.5	3.8	11.6	7.8

* To conform to the level of the right auricle, 5.0 cm. should be added to these figures.

TABLE 2—*Continued*

Number of measurements	Date	Name	Age	Surface area	Pulse rate	Vital capacity	Vital capacity per square meter	Arterial pressure		*Venous pressure H_2O	Circulation time			Circulation time per square meter		
								Systolic	Diastolic		Arm to heart	Arm to arm	Pulmonary	Arm to heart	Arm to arm	Pulmonary
	1926			*square meter*		*cc.*	*cc.*	*mm.*	*mm.*	*cm.*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*	*seconds*
378	February 23	J. M.	21	1.84	66	4,900	2,662	110	76	−1.0	8.0	19.0	11.0	4.3	10.3	5.9
380	February 23	J. G.	54	1.78	63	3,500	1,967	165	80	+6.0	11.5	22.0	10.5	6.4	12.0	5.9
382	February 26	P. M.	21	1.57	67	4,100	2,611	126	64	−1.0	4.5	15.5	11.0	2.8	9.8	7.0
383	February 26	P. M.	21	1.57	76	4,100	2,611	126	64	−0.5	6.5	18.5	12.0	4.1	11.7	7.6
385	March 9	R. P.	24	1.84	54	4,700	2,555	122	72	+6.5			16.0			8.7
386	March 9	J. R.	27	1.91	71	5,150	2,690	114	74	+3.0	11.0	22.0	11.0	5.7	11.5	5.7
388	March 11	E. C.	33	1.67	63	4,500	2,695	120	74	+5.0	9.0	21.0	12.0	5.3	12.5	7.1
390	March 16	A. W.	22	1.66	60	4,200	2,529	106	68	+18.0	14.0	26.0	12.0	8.4	15.6	7.2
391	March 16	F. D.	41	1.62	55	3,650	2,251	94	50	+3.5	13.0	25.0	12.0	8.0	15.4	7.4
392	March 16	A. W.	22	1.66	63	4,200	2,529	106	68	+6.5	6.5	20.5	14.0	3.9	12.3	8.4
394	March 16	J. F.	31	1.71	125	3,700	2,162	118	74	−2.0	2.5	8.0	5.5	1.4	4.6	3.2
395	March 16	V. F.	46	1.74	70	3,350	1,925	124	72	−4.0	6.5	20.5	14.0	3.7	11.7	8.0
400	March 21	H. B.	36	1.51	78	2,900	1,921	112	60	−2.0	7.0	20.0	13.0	4.6	13.2	8.6
401	March 21	W. C.	51	2.13	72	3,400	1,596	126	80	+4.5	9.0	21.0	12.0	4.2	9.8	5.6
402	March 21	H. B.	36	1.51	79	2,900	1,921	112	60	−1.5	6.0	21.0	15.0	3.9	13.9	9.9
416	April 21	J. Q.	46	1.70	64	3,350	1,970	128	82	−1.0			17.5			10.3

* To conform to the level of the right auricle, 5.0 cm. should be added to these figures.

of blood flow in the aorta of man may be 144 to 216 mm. per second. R. Tigerstedt (18), basing his estimate on different anatomical data, states that in the aorta it is from 75 to 90 mm. per second. Although no reliable data concerning the velocity of blood flow in the arteries are available, the time of transit through the large arteries must be relatively short compared to the pulmonary circulation time and the variations in arterial velocity from normal person to normal person must be relatively small.

Actual measurement of the time of entrance of the active deposit into the left chambers of the heart has not so far been possible. Fortunately, as will be shown, measurement of the velocity of the venous blood to the right chambers of the heart affords a valuable basis for estimating the velocity of the arterial blood flow from the left ventricle to the antecubital arteries. In general, the volume blood flow into the right auricle through the inferior and superior vena cava must equal the volume of blood flowing through the systemic aorta in a corresponding interval of time. Since the total cross sectional area of the big veins near the heart is about twice that of the root of the aorta, the velocity of the blood in the great veins will be approximately half that of the aorta. Similar considerations apply to the relation between other large veins and arteries. If the path from the point of injection to the right heart is considered analogous to the path traversed by the active deposit from the left chambers of the heart to the antecubital region of the other arm, as it is in our tests, the circulation time of the venous path will in general be twice as long as the circulation time of the analogous arterial path. We have therefore taken half the general average of the venous circulation time to the right chambers of the heart and subtracted it from the "crude pulmonary circulation time" to give the "derived pulmonary circulation time". The arterial velocity correction is 3.3 seconds (that is to say, half the venous velocity time of 6.6 seconds), which subtracted from the general average crude pulmonary circulation time (10.8 seconds), leaves 7.5 seconds as the average derived pulmonary circulation time. This time measures the time necessary for the radium active deposit to flow through the chambers of the heart as well as through the pulmonary circulation, and may therefore vary to a slight degree according to the phase of the cardiac cycle in which the active deposit enters the auricles

and ventricles. If the active deposit enters the auricle just before ventricular systole the time lost in the heart will be practically nil, whereas if the radium active deposit enters the auricle at the beginning of venticular diastole the time lost in the heart may be one second if the heart rate is approximately sixty. Since similar considerations apply to both sides of the heart, it is conceivable though hardly probable, that the circulation time might be prolonged nearly two seconds. Since the time lost in the heart may vary from 0 to 2 seconds, one may consider one second as the average time of transit through the chambers of the heart. One second, therefore, should be subtracted from the derived pulmonary circulation time to give the actual pulmonary circulation time. In our observations, then, 6.5 seconds measures the average time necessary for the active deposit to appear in the left auricle after its previous entrance into the pulmonary artery.

RESULTS

The significance of the pulmonary circulation time and its relation to the minute volume output of the heart and to the amount of blood in the lungs. As stated above, the pulmonary circulation time refers to the time necessary for a given particle of blood to appear in the left auricle after its previous entrance into the pulmonary artery. This time measures the interval necessary for the fastest particle of a foreign substance to traverse the shortest available path between the point of injection and the place of detection. If the vascular pathways were all equal the pulmonary circulation time would signify the interval necessary for the displacement of the blood in the lungs, and would be a measure of the mean velocity. On the other hand, if there are considerable variations in the different pathways of the pulmonary circuit, or if there is a hastening on of the central stream, the pulmonary circulation time would have no necessary relation to the amount of blood displaced in the lungs, and its significance would therefore be lessened. The work of G. N. Stewart (4), as well as some observations discussed in a previous communication (10), indicate that the pulmonary circulation time is an index of the mean pulmonary blood velocity. G. N. Stewart found that, following the injection of dyes into the external jugular vein, there was no stringing out of the dye after it had traversed the pulmonary capillaries and had entered the

carotid artery. This observation lends support to the concept of the equality of the available pulmonary vascular pathways. Similarly, G. N. Stewart has pointed out (19) that the mean pulmonary circulation time bears a definite relation to the quantity of blood in the lungs and the minute volume flow through the lungs. This relation may be expressed by the formula $V = Q\frac{60}{T}$, where V is the volume output of the heart per minute in liters, Q is the quantity of blood in the lungs in cubic centimeters, and T is the mean pulmonary circulation time in seconds. If two of these unknown quantities are measured the third can be ascertained. According to the relation expressed by the above formula, the pulmonary circulation time will vary directly with the amount of blood in the lungs and inversely with the minute volume flow through lungs. An increase in the pulmonary circulation time signifies a preponderant increase in the amount of blood in the lungs compared to the minute volume output of the right ventricle. Since the pulmonary circulation time reflects changes in either or both these two factors it is of the utmost importance in expressing their balance under various conditions in health and disease. The use of the pulmonary circulation time as T in this formula depends on the assumption that the pulmonary circulation time is identical with the mean velocity. On the other hand, if the vascular pathways are dissimilar or if there is considerable hastening on of the axial stream; T, in the formula would be too low and the amount of blood in the lungs would become impossibly small.

The general average of the actual pulmonary circulation times presented in the preceding tables is 6.5 seconds. The table below (table 3) is a summary of measurements of the minute volume output of the heart in normal males lying at rest as found by various observers. Measurements of the minute volume output of the heart, available from the literature, performed with the subjects in sitting position are not comparable to our data.

The average of the minute volume output found by these two different methods in normal resting males is 6.38 liters. Applying the above mentioned equation $V = Q.\frac{60}{T}$, $6.38 = Q.\frac{60}{6.5}$ or Q, the amount of blood in the lungs equals 589 cc. It is interesting in the

light of this finding which is the first approximation by actual measurements during life of the amount of blood in the lungs of man, to learn

TABLE 3

Minute volume of heart in normal males lying at rest as obtained from literature

Subject	Minute volume output	Observers
	cc.	
A. V. B.	5.45	H. Field and A. V. Bock (20, 21)
H. F.	10.90	
A. C. R.	7.14 (8.9, 5.38)	
J. R. L.	9.00	
W. A. Mc.	8.10	
T. M. M.	6.70	
S. A. O.	8.10	
F. W. L.	6.55	
C. M. J.	7.30	
F. T. H.	4.81	
J. M. F.	7.17	
W. L. McK.	6.72	
W. B. C.	7.28	
P. D.	7.80	
A. M. B.	8.34	
J. C. E.	8.51	
M. E. M.	5.13	
M. F. H.	6.63	
M. A. S.	7.46	
S. L. W.	5.35	
H. P. S.	9.03	
H. N. S.	5.90	
A. K.	6.63	
E. F. G.	9.23	
G. C. R.	4.70	
Average	7.19	
Male	5.65	Lindhard (22)
Male	5.30	
Male	7.20	
Male	4.20	
Average	5.57	

the amounts surmised by various observers in the past. Spehl and Desquin (23) found in eight rabbits that the pulmonary blood volume at the end of inspiration was 8.3 per cent of the total blood volume.

Y. Kuno (24), working on heart lung preparations of dogs and calculating total blood volume as 7 per cent of the body weight, found that the volume of the blood in the lungs varied between 8.8 and 19.6 per cent with an average of 12 per cent of the total blood volume. G. N. Stewart (4) found in two dogs in which both sides of the heart were obstructed simultaneously, that the lungs contained 21 and 18.6 per cent of the total blood volume. Assuming, as did G. N. Stewart, that, as in the case of animals, the total blood volume of man is about one thirteenth of his body weight, and taking the average weight of the subjects as 70 kilos, the total blood volume would be 5.4 liters in which case 589 cc. would represent 11 per cent of the total blood volume. This observation is of importance not only in giving information in regard to the amount of blood in the lungs but also because it confirms the validity of the pulmonary circulation time as a measure of the mean velocity and at the same time indicates that the available pulmonary pathways are approximately equal. For if the mean velocity were much slower than the actual pulmonary circulation time observed, the value of Q would become impossibly large. Our finding of 589 cc. of blood as the average amount of blood in the lungs of man is in accord with the results of previous investigations on animals.

The relation of systemic blood pressure to the normal pulmonary circulation time. The effect, in animals, of changes of the systemic arterial blood pressure upon the pulmonary circulation of animals has been studied by various observers. Führer and Starling (25) working with the heart lung preparation, in which the cardiac rate and venous inflow were controlled, noted, in apparently vigorous hearts, that every elevation of systemic pressure caused a corresponding increase of pressure in the left auricle, the pulmonary artery and even in the right auricle. Similarly, Cloetta and Staubli (26) observed that compression of the thoracic aorta always caused increased lung volume and elevation of pulmonary arterial pressure. Straub (27) found that increased peripheral arterial resistance always produced passive pulmonary congestion as indicted by increased lung volume and increased left auricular pressure. Bradford and Dean (28) similarly observed that temporary compression of the aorta, or increased vasoconstriction, caused slight elevation of pulmonary arterial pressure. A rise of pres-

sure in the pulmonary circulation would not, of course, cause an increased velocity of blood flow unless the "head on" pressure, i.e., the pressure gradient, were greater. On the contrary, a simple increase in pressure, by distending the elastic pulmonary bed and increasing the amount of blood in the lungs, would lead to a lengthened pulmonary circulation time. It seemed of interest to compare the pulmonary circulation times in those individuals who showed the highest and lowest blood pressures (table 4).

These results show no evident relation between normal variations in pulmonary circulation time and normal variations in systemic blood pressure. Back pressure effects either do not occur normally in man, or if they do occur, any increase in the amount of blood in the lungs is

TABLE 4

Blood pressure and pulmonary circulation time

Patient Number	Blood pressure		Pulmonary circulation time	Patient Number	Blood pressure		Pulmonary circulation time
	Systolic	Diastolic			Systolic	Diastolic	
	mm. Hg.	*mm. Hg.*	*seconds*		*mm. Hg.*	*mm. Hg.*	*seconds*
255	166	94	5.5	279	98	56	3.5
286	174	84	3.0	280	78	54	6.5
250	140	70	9.5	317	92	70	4.5

attended by a proportionate increase in the minute volume flow of blood.

Conditions which may account for the variations in pulmonary circulation time of healthy men. The pulmonary circulation time may conceivably be influenced according to the phase of respiration during which the active deposit enters the heart and pulmonary vessels. We have not had the opportunity to investigate this particular point although repeated measurements in the same person show that such an influence, if present, can hardly be of clinical or physiological significance. This is in accord with the observations of E. K. Marshall (29) who found that changes of 100 per cent or more in the ventilation of the lungs were not accompanied by changes in the minute volume output of the heart in trained unanesthetized dogs.

The relation between the ventricular rate of the heart and the velocity of blood flow through the lungs. The data in table 5 indicate that an

increased ventricular rate is associated with a slightly though definitely increased velocity of blood flow, although this relation does not obtain in each instance. In this connection patient J. F. (394, table 2), who was suffering from post-traumatic neurosis, is of particular interest. Although he was coöperative his pulse rate was 125 and he showed the signs of excitement. The venous flow time was 2.5 seconds and the crude pulmonary circulation time was 5.5 seconds. Applying the considerations previously discussed, but using the patient's own venous time and ventricular rate, because of the con-

TABLE 5

Ventricular rate and pulmonary circulation time

Ventricular rate 90+			Ventricular rate 70−		
Patient number	Pulse	Pulmonary circulation time (crude)	Patient number	Pulse	Pulmonary circulation time (crude)
		seconds			*seconds*
256	97	11.5	250	62	13
260	94	9	253	69	10
263	102	10	266	52	13
275	105	7	280	69	10
279	94	7	285	70	13
286	98	6.5	288	68	10.5
289	92	7.5	297	62	9
310	94	7.5	320	66	11.5
313	92	12			
317	100	8			
	125	5.5			
Average....	96.8	8.4		65	11.2

spicuous deviation from the average, his actual pulmonary circulation time was 3.8 seconds. This is the shortest actual pulmonary circulation time so far observed. In our previous study (7) of the normal arm to arm circulation time an increase in the pulse rate was likewise associated with a slight but definite increase in the velocity of blood flow.

The influence of age on the velocity of blood flow through the lungs. According to the measurements of the pulmonary circulation tabulated (table 2), the velocity of blood flow through the lungs showed no constant relation to the age of the patient. This is in accord with our

previous observations on the arm to arm circulation times according to which the velocity of blood flow expressed the actual condition of the circulation independent of the age of the patient. In a few young persons, in whom the ventricular rate was elevated, the velocity of blood flow was somewhat increased.

The influence of the venous pressure on the velocity of blood flow through the lungs. Whether high venous pressure as observed in the antecubital vein of the arm is associated with an increase in the velocity of venous blood to the heart and through the lungs depends on the cause of the increase in pressure. Were the increase in pressure due to obstruction or pressure on the vein, or to vasomotor constriction with consequent undue closure of the venous valves or to circulatory failure, one would expect a retardation in the velocity of blood flow. For in all these instances the pressure increase is due to lessened outflow from the vein rather than to increased inflow. In certain persons who appeared perfectly normal, though somewhat excitable, the venous pressure was unusually high and the velocity of venous blood flow to the right heart chambers was considerably retarded (nos. 311, 313, 314, table 2). In a few instances this venous slowing has been associated with undue prolongation of the pulmonary circulation time.

The relation between the surface area and the velocity of blood flow. The heat production and also the vital capacity of the lungs bear definite relations to the surface area in man. These measurements express a relation between absolute quantities and surface area. The velocity of blood flow as reported in these communications does not refer to velocity of flow in actual units of time and distance but rather to the time necessary for the active deposit of radium to travel between certain arbitrarily chosen points. If, in large persons, the distance between the two arbitrarily chosen points were proportional to the increase in surface area and the velocity of blood flow in absolute units of time and distance were to remain unchanged, increased surface area would be associated with increase in the pulmonary circulation time. That the circulation times as measured by our method did not show any definite relation to the surface area indicates that the time of transit is independent of the distance between the arbitrarily chosen points.

SUMMARY

1. The radium C method makes possible for the first time the measurement in man of the velocity of blood flow through the lungs.

2. The method described measures also the velocity of the venous blood from the arm to the right chambers of the heart.

3. The crude pulmonary circulation time in sixty-two measurements on normal resting individuals varied from five to seventeen seconds. The average crude pulmonary circulation time was eleven (10.8) seconds.

4. The circulation time of the venous blood from the right elbow to the right auricle varied from two to fourteen seconds with an average of seven (6.7) seconds.

5. Repeated measurements in the same individuals showed a maximum variation in the crude pulmonary circulation of three and a half seconds with an average of two seconds while the maximum variation in the venous flow time was seven and a half seconds, with an average of three seconds.

6. The variations in the velocity of blood flow through the lungs in the same individuals at different times and in different individuals are less than that observed in the velocity of the venous blood of the arm.

7. No definite relation was observed between velocity of pulmonary blood flow and age of the patient.

8. With a conspicuous increase in the pulse rate there is a slight but definite increase in the velocity of blood flow through the lungs.

9. Normal variations in systemic arterial or venous blood pressure bear no relation to normal variations in velocity of blood flow through the lungs.

10. The average actual pulmonary circulation time observed by us was 6.5 seconds; the average minute volume flow through the lungs as observed by others was 6.38 liters. According to the formula $Q = \frac{TV}{60}$ and applying the pulmonary circulation time as mean velocity, T, the amount of blood in the lungs of man averages 589 cc. or 11 per cent of the total blood volume.

11. The fact that the proportion of blood in the lungs of man so calculated conforms to that found experimentally in animals indicates that the pulmonary circulation time is a measure of the mean

velocity of blood flow through the lungs and that the available pulmonary pathways are about equal.

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