STUDIES ON THE EFFECT OF CARDIAC IRREGULARITY ON THE CIRCULATION: *I. The Relation of Pulse Deficit to Rate of Blood Flow in Dogs Subject to Artificial Auricular Fibrillation and to Regular Tachycardia*

Harold J. Stewart, … , J. Hamilton Crawford, A. R. Gilchrist

J Clin Invest. 1928;5(2):317-333. https://doi.org/10.1172/JCI100162.

STUDIES ON THE EFFECT OF CARDIAC IRREGULARITY ON THE CIRCULATION

I. The Relation of Pulse Deficit to Rate of Blood Flow in Dogs Subject to Artificial Auricular Fibrillation and to Regular Tachycardia

By HAROLD J. STEWART, J. HAMILTON CRAWFORD and A. R. GILCHRIST

(From the Hospital of the Rockefeller Institute for Medical Research, New York City)

(Received for publication July 8, 1927)

In preceding papers (1, 2) we have reported observations concerning the effect of regular and irregular tachycardia (auricular fibrillation) on the rate of blood flow in normal unanesthetized dogs.

The terms "rate of blood flow" and "relative blood flow" have been used in these investigations (1, 2) to denote specific functions. The *rate of blood flow* refers to the arterio-venous difference in oxygen. The difference corresponds to the tissue utilization of this gas. The volume of gas which the tissues take depends of course on the volume of blood which passes them. If their requirements (that is to say, metabolism) remain constant, the amount of oxygen taken must remain constant, provided that the volume of the blood and the partial pressure of the gases in it, also remain constant. We infer that if the arterio-venous difference changes, either by increase or by diminution, the volume of blood which passes the tissues must have changed, for there is no reason to believe that there has been change in any of the other possible factors. Obviously, the data do not permit definitive inferences to be drawn on the cardiac output, for we lack knowledge in these experiments of the amount of oxygen which has been breathed. We have taken in a given animal, the arterio-venous difference to represent 100, when the mechanism of his heart beat is normal. We have also estimated it under the conditions developed by various abnormal rhythms and have found a ratio between the normal and the abnormal figures. This ratio we call *relative blood flow*. If, for

instance, the arterio-venous oxygen difference is 1.5 mM. during a normal period and increases to 3.0 mM. during an artificial rhythm, the rate of flow during the artificial rhythm must have been slower during the second period. The ratio between the two then is 1.5/3.0 or 50 per cent.

It was found that the rate of blood flow was uniformly deceased in auricular fibrillation. In regular tachycardia, on the other hand, the rate of blood flow was unchanged in two-thirds of the observations, but in one-third it was decreased. Why the rate of blood flow was unchanged in some dogs during regular tachycardia and decreased in others was not evident from the data which we had. On reflection, it appeared that the difference is not due to absolute increase in heart rate for we have increased the regular rate to 390 per minute without changing the rate of blood flow, while on other occasions a decrease occurred during rates of 250 to 280 per minute. Nor does it seem to be due to the percentile increase in rate. For instance, an increase of 50 per cent was followed by a decrease in rate of blood flow; while an increase of 129 per cent occurred without any change; that is to say an increase of 50 per cent or 100 per cent may leave the blood flow unchanged or bring about a decrease (2). The difference may, of course, lie in differences in the hearts themselves, for the response of one heart to approximately the same stimuli is not always the same as that of another. Such differences cannot, however, now be detected by measurement. It occurred to us that the presence of ineffective beats (the pulse deficit) might be one of the factors concerned in bringing about a change in the rate of blood flow which has been found in our experiments. This factor occurred to us as a possibility because we are already familiar with its occurrence in rapid auricular fibrillation in patients. We have therefore correlated in a series of experiments the rate of blood flow with the pulse deficit in regular and irregular tachycardia in the same dog. These experiments form the subject of this paper.

METHODS

The operative procedure used in the preparation of the dogs and the method of investigation were described in preceding papers (1, 2). Briefly, wire electrodes were sutured to the right auricles. The operations were performed with sterile

precautions. The dogs were anesthetized with ether given by the intratracheal method. After the dogs recovered from the preliminary operation the heart was stimulated through these electrodes and the effect of the new rhythm on the rate of blood flow was studied. Irregular tachycardia (auricular fibrillation) was brought about by means of a faradic current. Regular tachycardias were maintained by means of single induced break shocks thrown into the auricle at a regular rapid rate, which could be varied as desired. The apparatus which we used to obtain these stimuli was described in a previous paper (2). In order to calculate the pulse deficit we have recorded simultaneously on the same film the electrocardiogram and a tracing of the femoral pulse. The femoral pulse was transmitted by rubber tubing from a rubber cuff applied to the right hind leg through the Kolls and Kubie modifications of the Erlanger capsule (3, 4) to a Frank capsule placed in front of the camera. The rubber cuff on the leg was inflated with air to a pressure near the diastolic level. The movements of a beam of light focused on the mirror glued to the membrane of the Frank capsule were reflected to the lens of the camera and were traced on the moving sensitive film.

The oxygen content of four samples of arterial and of mixed venous blood (5, 6) was estimated by the Van Slyke and Neill manometric method (7) and the relative blood flow calculated The first samples were taken during the period of normal rhythm; the second, after auricular fibrillation had been present for one hour and while it was still present; the third, one to two hours after the return to the normal rhythm; and the fourth, one hour after the onset of regular tachycardia maintained artificially near the same ventricular rate as that found during the fibrillatory period. The pulse deficits were calculated from simultaneous electrocardiograms and femoral pulse tracings taken at the time the blood samples were drawn. In some animals the observations were made first during regular tachycardia while in others first during the period of fibrillation, but a rest period of one to two hours intervened between the two sets of observations in order to avoid confusion from the effect of the two mechanisms on the blood flow. As before, the dogs lay quietly on the table without anesthesia and were so far as we know in a basal metabolic state on the day of the experiment. Under these conditions we have, as has been said, interpreted changes in the oxygen consumed per liter of blood (that is to say, the difference between the oxygen content of the arterial and of the mixed venous blood) as representing changes in rate of blood flow and not to changes in metabolism. And the ratio of the oxygen consumed in the two periods gives therefore the relative blood flow. We did not attempt to estimate the oxygen absorption of the dogs because of the wide variation in results obtained in untrained, unanesthetized dogs. The basal oxygen consumption of an untrained dog presumably does not differ from that of the same dog lying in the same position after training. The untrained dog, however, reacts to the procedure used in measuring the oxygen consumption by emotional disturbances with attendant changes in oxygen consumption, while one trained to those procedures is not disturbed by them. We have estimated the oxygen consumption in a few trained

TABLE 1

The correlation of rate of blood flow and pulse deficit in auricular fibrillation in dogs

Dog number	Weight	Time with reference to stimulation	O_2 content		Arteriovenous oxygen difference*	Blood flow per cent of initial	Decrease blood flow	O_2 capacity	O_2 saturation†		Rhythm	Duration of stimulation	Heart rate (electrocardiogram)	Femoral pulse rate	Pulse deficit	Duration of rest after stimulation
			Arterial	Mixed venous					Arterial	Mixed venous						
	kgm.		*mM.*	*mM.*	*mM.*	*per cent*	*per cent*	*mM.*	*per cent*	*per cent*		*minutes*	*per minute*	*per minute*	*per minute*	*hours*
1	14.7	Before	11.15	7.91	3.24	100		12.08	91.5	65.1	N. R.‡		230	230	0	
		During	10.68	6.64	4.04	80	20	11.81	90.0	56.0	A. F.§	60	290	240	50	
		After	10.72	6.03	4.69	69	31	11.59	91.7	51.7	A. F.¶		310	240	70	2⅓
2	17.3	Before	10.94	7.82	3.12	100		12.67	85.6	61.4	N. R.		150	150	0	
		During	11.61	7.59	4.02	78	22	12.65	91.0	59.6	A. F.	60	340–350	200–170	140–180	
		After	12.16	8.18	3.98	79	21	12.62	95.6	64.5	N. R.		150	150	0	2
3	13.5	Before	12.38	9.52	2.86	100		12.94	95.0	73.2	N. R.		180	180	0	
		During	12.71	7.92	4.79	59	41	13.38	94.3	58.8	A. F.	60	300	165	135	
		After	12.53	8.38	4.15	69	31	13.03	95.5	64.0	N. R.		180	180	0	1½
4	14.8	Before	11.25	8.17	2.99	100		11.81	94.5	77.3	N. R.		190	190	0	
		During	11.80	6.72	5.08	59	41	12.04	97.2	55.5	A. F.	60	340–350	160–150	180–200	
5	13.9	Before	10.47	7.14	3.33	100		9.76 A** 9.84 V	100.0	72.2	N. R.		230	230	0	
		During	10.56	5.29	5.27	63	37	10.75	97.4	49.8	A. F.	60	340	190	150	
6	10.2	Before	11.10	8.36	2.74	100		11.21	98.2	74.2	N. R.		140	140	0	
		During	11.21	6.84	4.37	62	38	11.40	97.5	59.6	A. F.	60	340	210	130	
7	13.5	Before	9.57	5.88	3.69	100		9.35	100.0	62.4	N. R.		80	80	0	
		During	9.84	5.12	4.72	78	22	9.76	100.0	52.0	A. F.	60	340	160	180	

8	11.0	Before	11.09	8.84	2.25	100		11.88	92.6	74.0	N. R.		160	160	0
		During	11.70	6.77	4.93	46	54	11.90	97.5	56.5	A. F.	60	300	180	120
9	10.5	Before	9.00	5.91	3.09	100		9.53	93.5	61.5	N. R.		140	140	0
		During	8.67	4.19	4.48	69	31	9.00	95.3	46.1	A. F.	60	320	200	120
10	12.2	Before	10.09	6.49	3.60	100		10.83	92.3	59.5	N. R.		170	170	0
		During	10.14	4.89	5.25	68	32	10.55	95.3	45.9	A. F.	60	330	190	140

* Oxygen removed from each liter of blood.

† Before calculating the oxygen saturations, 0.09 mM. and 0.04 mM. O_2 (the amounts of oxygen in physical solution) were subtracted from the arterial and mixed venous oxygen contents respectively.

‡ N. R. = normal rhythm.

§ A. F. = auricular fibrillation.

¶ Spontaneous auricular fibrillation was still present 2⅓ hours after faradic stimulation had been discontinued.

** A = arterial blood; V = mixed venous blood.

TABLE 2

The correlation of rate of blood flow and pulse deficit in regular and irregular tachycardia (auricular fibrillation) in dogs

Dog number	Weight	Time with reference to stimulation	O_2 content		Arterio-venous oxygen difference*	Blood flow per cent of initial	Change in blood flow†	O_2 capacity	O_2 saturation‡		Rhythm	Duration of stimulation	Heart rate (electrocardiogram)	Femoral pulse rate	Pulse deficit	Duration of rest after stimulation
			Arterial	Mixed venous					Arterial	Mixed venous						
	kgm.		*mM.*	*mM.*	*mM.*	*per cent*	*per cent*	*mM.*	*per cent*	*per cent*		*minutes*	*per minute*	*per minute*	*per minute*	*hours*
11	10.6	Before	10.59	7.05	3.54	100		10.80	97.1	64.9	N. R.§		100	100	0	
		During	10.69	8.34	2.35	150	+50	11.12	95.3	74.6	A. N. R.¶	60	170††	170	0	
		Before	10.62	8.16	2.46	100		11.18	94.2	72.6	N. R.		120	120	0	2¼
		During	10.90	7.40	3.50	70	−30	11.08	97.5	66.4	A. F.**	60	300	140	160	
12	13.5	Before	8.30	6.63	1.67	100		9.23	89.0	71.4	N. R.		150	150	0	
		During	8.06	6.27	1.79	93	−7	8.78	90.7	71.0	A. N. R.	60	310†† 340	310 340	0 0	
		Before	7.98	6.25	1.73	100		8.70	90.7	71.3	N. R.		160	160	0	2
		During	7.30	4.51	2.79	62	−38	8.14	88.7	55.0	A. F.	60	280 300 270	280 220 230	0 80 40	
13	18.6	Before	12.48	8.44	4.04	100		12.76	97.1	65.8	N. R.		140	140	0	
		During	12.34	7.90	4.44	90	−10	13.09	93.6	60.0	A. N. R.	60	330	330	0	
		Before	12.48	9.00	3.48	100		12.81	96.7	69.9	N. R.		180	180	0	2½
		During	12.38	7.22	5.16	67	−33	13.35	92.0	53.7	A. F.	60	300	180	120	
14	14.9	Before	11.14	7.34	3.80	100		12.10	91.3	60.3	N. R.		170 170 170	170 170 170	0 0 0	
		During	11.12	7.25	3.87	98	−2	11.69	94.4	61.7	A. N. R.	60	370 370 370	370 370 370	0 0 0	

		Before	11.06	8.06	3.00	100		11.54	95.1	69.5	N. R.		200 200	200 200	0 0	2
14 cont.	14.9	During	10.47	5.01	5.46	55	−45	11.27	92.1	44.1	A. F.	60	290 320 300 340 320	220 200 190 220 220	70 120 110 120 100	
		Before	9.07	7.26	1.81	100		9.77	91.9	73.9	N. R.		100 100	100 100	0 0	
15	12.0	During	9.43	7.10	2.33	78	−22	9.90	94.3	71.3	A. N. R.	60	350 350 350 350	175 350 175 350	175 0 175 0	
		Before	9.03	6.97	2.06	100		9.55	93.6	72.5	N. R.		120 120	120 120	0 0	2½
		During	9.40	5.72	3.68	56	−44	9.89	94.1	57.4	A. F.	60	360 380	180 200	180 180	
		Before	10.66	7.97	2.59	100		11.32	93.4	70.0	N. R.		140	140	0	
16	23.7	During	11.16	6.87	4.29	60	−40	11.69	94.7	58.4	A. F.	60	320 210	160 130	160 80	
		Before	10.46	6.78	3.68	100		10.66	97.2	63.2	N. R.		170	170	0	3
		During	10.16	4.28	5.88	75	−25	10.31	97.7	41.1	A. N. R.	60	320	160	160	

* Oxygen removed from each liter of blood.

† In this column + indicates increase and − decrease.

‡ Before calculating the oxygen saturations, 0.09 mM. and 0.04 mM. O_2 (the amounts of oxygen in physical solution) were subtracted from the arterial and mixed venous oxygen contents respectively.

§ N. R. = normal rhythm.

¶ A. N. R. = artificial normal rhythm.

** A. F. = auricular fibrillation.

†† Occasionally the heart is not responding to all the stimuli.

dogs during these experiments and found that the metabolism of the dogs remains constant (8). The calculations designated relative blood flow made in this paper and the two preceding ones (1, 2) are therefore valid, in so far as the assumption is made that the changes which were observed depend on changes in the rate of blood flow and not on changes in the rate of metabolism.

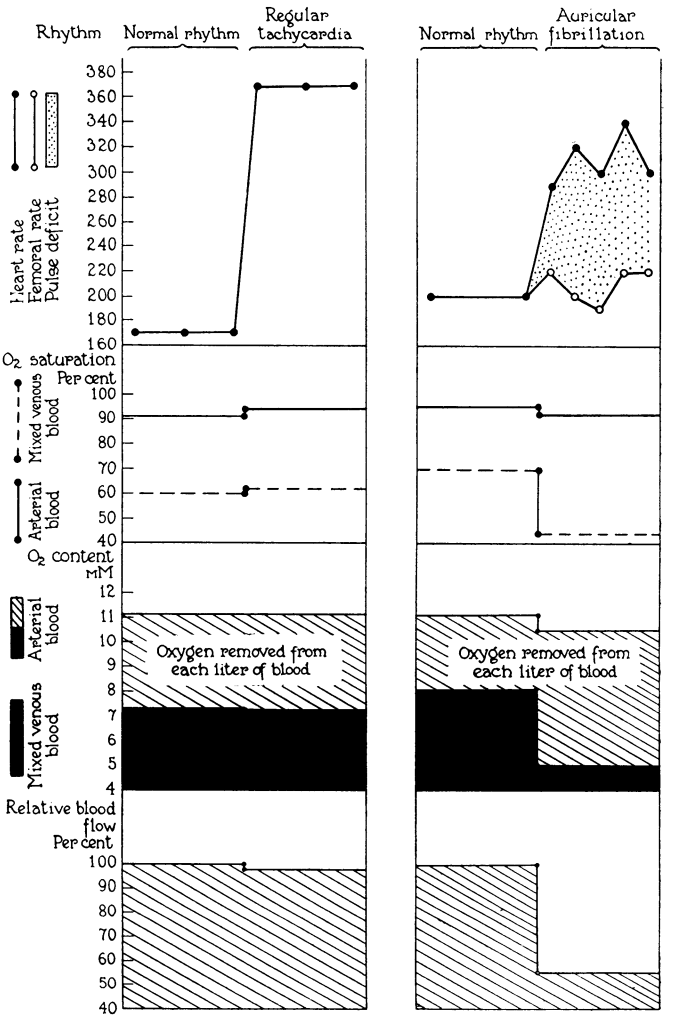

FIG. 1. IN THIS FIGURE IS COMPARED THE EFFECT OF REGULAR AND OF IRREGULAR TACHYCARDIA UPON THE RATE OF BLOOD FLOW AND THE OCCURRENCE OF THE PULSE DEFICIT IN DOG 14

OBSERVATIONS

The correlation of the rate of blood flow and pulse deficit in auricular fibrillation

There are 10 sets of observations on 10 dogs (table 1). In all there was a decrease in rate of blood flow ranging from 20 to 54 per cent during the fibrillatory period. During the natural normal rhythm all the beats were effective, but during the period of auricular fibrillation there were pulse deficits ranging between 50 and 200 per minute, the ventricular rates ranging between 290 and 350 per minute.

A comparison of the effect of auricular fibrillation and regular tachycardia in the same dog

In 6 dogs we have observations on the rate of blood flow and the pulse deficit during regular tachycardia as well as during auricular fibrillation (table 2). The rate of blood flow in dog 14 was unchanged during the regular tachycardia; there was no pulse deficit even when the heart was beating at a rate of 370 per minute (fig. 1). During auricular fibrillation the rate of blood flow was decreased 45 per cent but there was a pulse deficit of 70 to 120 per minute, the ventricular rate varying between 290 and 340 per minute. The rhythms which obtained at the time the blood samples were taken in this dog were recorded electrocardiographically with simultaneous tracings of the femoral pulse (fig. 2). Similar results were obtained in 4 (dogs 11, 12, 13 and 14) of the 6 dogs.

In dog 15 there was a decrease in rate of blood flow of 44 per cent during auricular fibrillation, the ventricular rate being 360 to 380 per minute; there was a pulse deficit of 180 per minute (fig. 3). During regular tachycardia at the same ventricular rate (350 per minute) the rate of blood flow was, however, likewise *decreased* (22 per cent). The unexpected decrease may be explained by the fact that at times all the beats were effective, while at other times only every other beat, that is to say, there was a pulse deficit of 175 per minute. The rhythms which were present at the time the blood samples were drawn were recorded electrocardiographically and simultaneous femoral

FIG. 2. ELECTROCARDIOGRAMS (LEAD II) OF DOG 14 ARE SHOWN AT THE TIME THE BLOOD SAMPLES WERE DRAWN

a was taken during the normal rhythm; *b* during regular tachycardia; *c* 2 hours after the end of the period of regular tachycardia and before auricular fibrillation was started; and *d* during auricular fibrillation. In this figure as well as in figures 4 and 5, *X* is the shadow of the electromagnetic signal and shows the frequency of the induced break shocks; *Y* is the electrocardiogram; *Z* is the femoral pulse tracing. A short time interval is seen between the beginning of the QRS complex of the electrocardiogram and the corresponding femoral pulse. This is due partly to the transmission time from the heart to the femoral artery and partly to the transmission time from the rubber cuff to the Frank capsule. In the femoral pulse tracing taken during auricular fibrillation (*d* curve *Z*) attention is called to the variation in the excursion of the femoral pulse from beat to beat. In this figure and in figures 4 and 5 divisions of the ordinates equal 10^{-4} volts; divisions of the abscissae equal 0.04 of a second. The original curves are sharply contrasted black and white; no half tones are lost by the method of reproduction. The curves are reduced to two-thirds of their natural size.

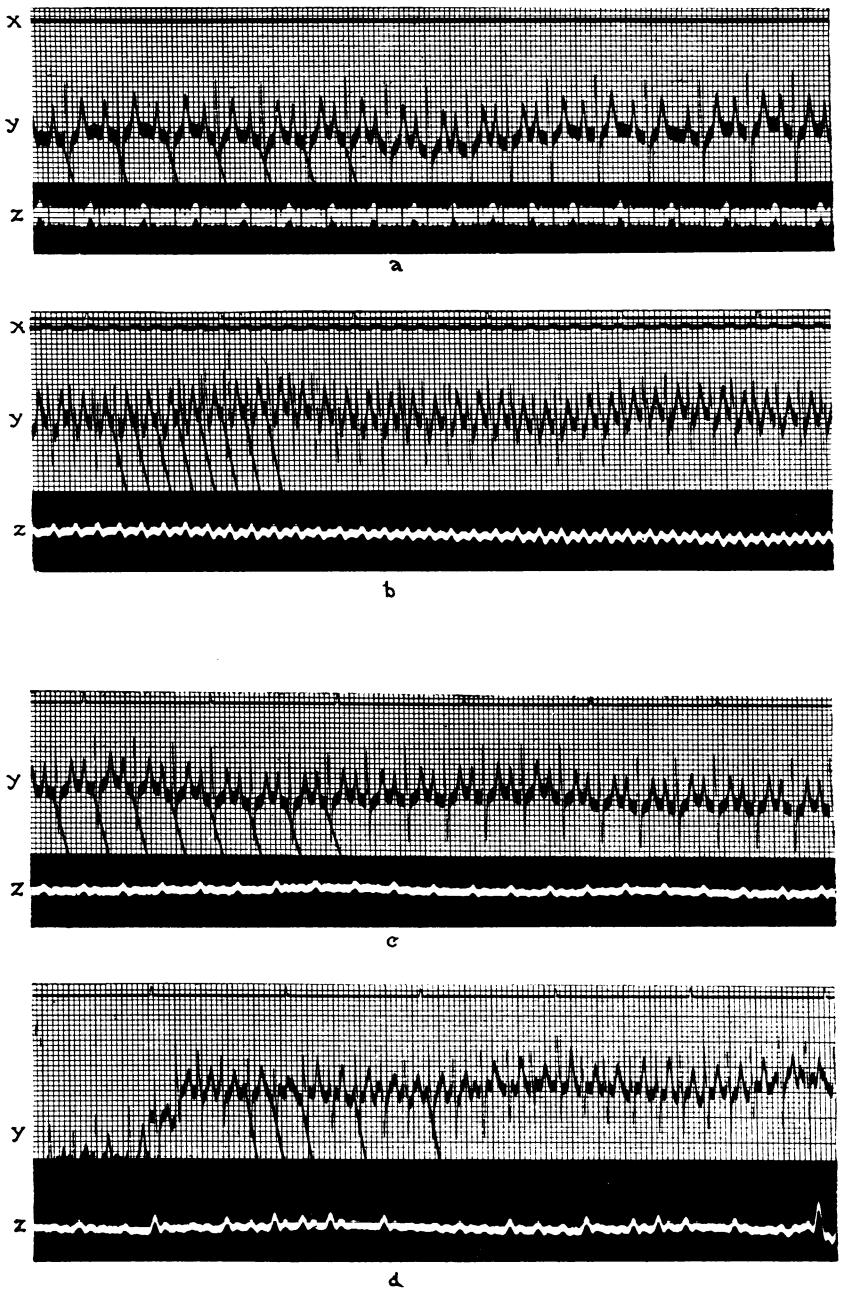

FIG. 2

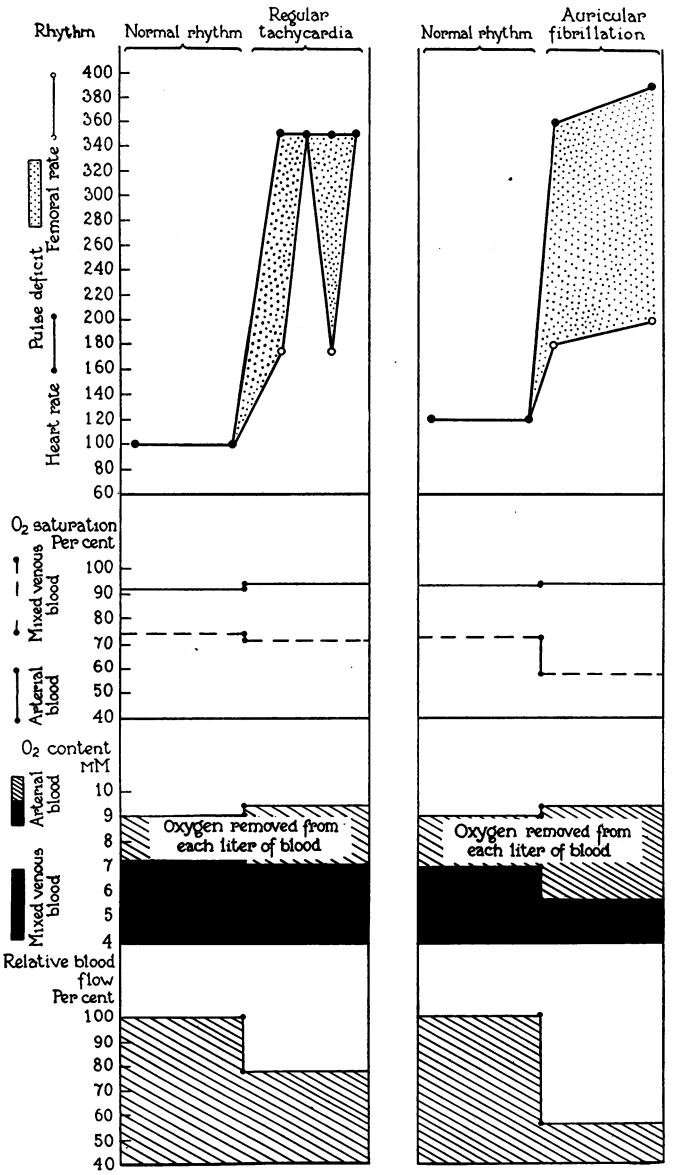

FIG. 3. IN THIS FIGURE IS COMPARED THE EFFECT OF REGULAR AND OF IRREGULAR TACHYCARDIA UPON THE RATE OF BLOOD FLOW AND THE OCCURRENCE OF THE PULSE DEFICIT IN DOG 15

FIG. 4. ELECTROCARDIOGRAMS (LEAD II) ARE SHOWN OBTAINED FROM DOG 15 *a* was made during the normal rhythm; *b* and *c* during the regular tachycardia; *d* 2½ hours after the end of the period of regular tachycardia and before auricular fibrillation was induced; and *e* at the *end* of the fibrillatory period. The reversion to the normal rhythm is shown. In curve *b* a pulse deficit occurs at every other beat, but in curve *c* all the ventricular beats are effective. The curves are reduced to two-thirds of their natural size.

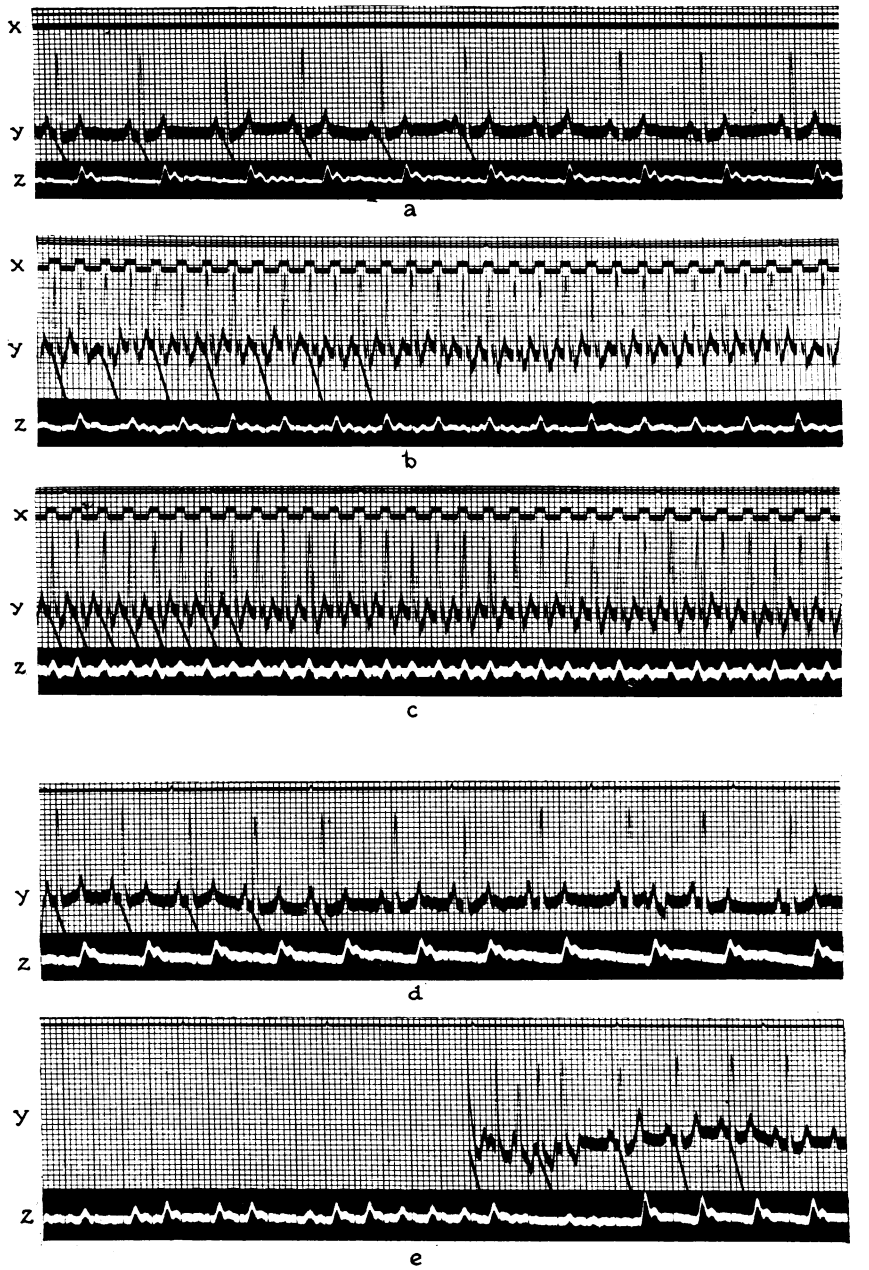

FIG. 4

pulse tracings made (fig. 4). A similar state was found to exist in the case of dog 16.

In 6 dogs, therefore, there was a decrease in rate of blood flow during auricular fibrillation and a pulse deficit was present in each instance.

TABLE 3

Summary of experiments correlating rhythm, pulse deficit and rate of blood flow

Dog number	Rhythm		Rate of blood flow			Pulse deficit	
	Rapid regular	Auricular fibrillation	Increase	No change	Decrease	Present	Absent
11	+		+				0
		+			+	+	
12	+			+			0
		+			+	+	
13	+			+			0
		+			+	+	
14	+			+			0
		+			+	+	
15	+				+	+	
		+			+	+	
16		+			+	+	
	+				+	+	
1		+			+	+	
2		+			+	+	
3		+			+	+	
4		+			+	+	
5		+			+	+	
6		+			+	+	
7		+			+	+	
8		+			+	+	
9		+			+	+	
10		+			+	+	

In 4 of these the rate of blood flow was *unchanged* during regular tachycardia and there was no pulse deficit. In the other two the rate of blood flow was decreased during this rhythm but a pulse deficit occurred. In short then, whenever the rate of blood flow decreased

in these experiments, whether in regular or irregular rhythms, a pulse deficit occurred (table 3).

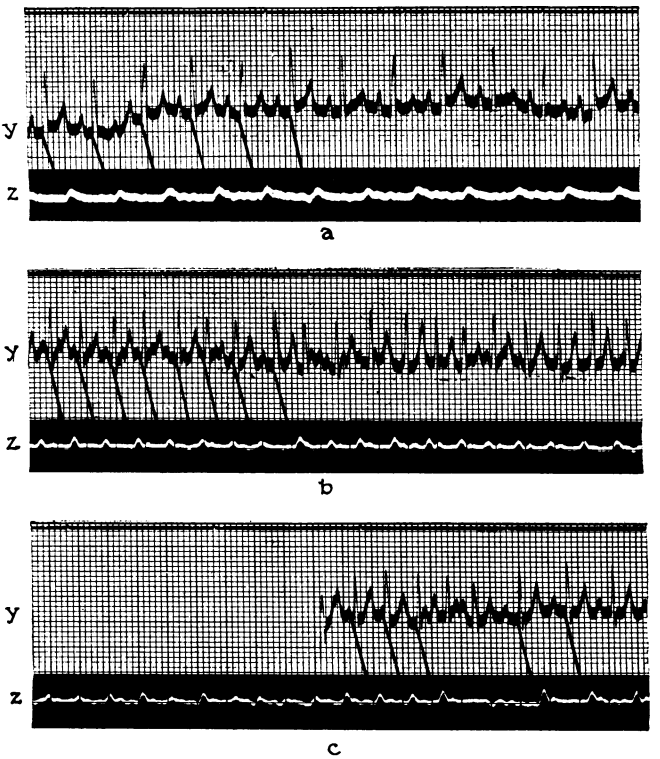

FIG. 5. ELECTROCARDIOGRAMS (LEAD II) ARE SHOWN OBTAINED FROM DOG 12

a was made during the normal rhythm; *b* during auricular fibrillation and *c* at the end of the fibrillatory period. The return to the normal rhythm is shown. In curve *b* all of the ventricular beats are effective while in *c* and other portions of the record there is an occasional pulse deficit. The curves are reduced to two-thirds of their natural size.

DISCUSSION

We have shown in these experiments that whenever a decrease in rate of blood flow occurred a pulse deficit was found to be present. The pulse deficit cannot, however, be the only factor involved, for in many instances when it was found, the number of beats which were

effective was still as large as during the normal slower rate. In dog 12 for instance (table 2, fig. 5) all the beats were effective in long stretches of the record, while here and there only a small pulse deficit occurred. We have no explanation to offer for this phenomenon, that is to say, the effectiveness of a certain number of beats at certain times and the ineffectiveness of the same number at others. In other cases not only were some beats wholly ineffective but there was also a variation in the degree of effectiveness of individual beats, as observed in differences in the excusion of the femoral pulse from beat to beat (figs. 2, 4 and 5). The inference which we draw on the nature of the influence of pulse deficit on rate of blood flow is that the intraventricular pressure developed during cardiac systole was either not great enough to open the aortic valves at all (pulse deficit) or was only sufficient to open the valves and to expel a small amount of blood, so that the net result so far as the propulsion of blood is concerned was a decrease. We do not know what factors were responsible for the decreased effectiveness of the beats. Among possible ones there may have been in the first place rapid rate combined with decreased ventricular filling, due to shortening of the diastolic period, and on this account decreased flow and output (8). In the second place, as we have previously shown (9), dilatation of the heart may have occurred sometimes to the extent that the muscle fibers attained a length greater than optimal so that the heart began to fail in output. In the third place, continuous rapid rates may have brought on a state of fatigue associated perhaps with a fall in aortic pressure, consequent decrease in the rate of coronary artery flow, followed by undernutrition of the muscle and decrease in contractile function. What part each of these factors played in the net result naturally cannot be estimated.

SUMMARY

The rate of blood flow and pulse deficit have been correlated in artifically induced regular and irregular tachycardia in normal unanesthetized dogs. It was found that:

1. During rapid auricular fibrillation the rate of blood flow was decreased and a pulse deficit was present.

2. During regular tachycardia there was no pulse deficit when the rate of blood flow was unchanged, but a pulse deficit was present when the rate of blood flow was decreased.

3. We have shown, what we supposed was the case, namely, that there is a positive correlation between rate of blood flow and pulse deficit.

CONCLUSIONS

In spite of the correlation which exists between pulse deficit and rate of blood flow in these experiments, there need be and there probably is no causal relation between them. Rather they both may occur as the result of the presence of one or more other factors such as decreased filling time, decreased aortic pressure and cardiac dilatation.

BIBLIOGRAPHY

1. Stewart, H. J., Crawford, J. H., and Hastings, A. B., J. Clin. Invest., 1926, iii, 435. The Effect of Tachycardia on the Blood Flow in Dogs. I. The Effect of Rapid Irregular Rhythms as Seen in Auricular Fibrillation.
2. Stewart, H. J., and Crawford, J. H., J. Clin. Invest., 1926, iii, 449. The Effect of Tachydardia on the Blood Flow in Dogs. II. The Effect of Rapid Regular Rhythm.
3. Kolls, A. C., J. Pharm. and Exper. Therap., 1920, xv, 443. An Indirect Method for the Determination of Blood Pressure in the Unanesthetized Dog.
4. Kubie, L. S., J. Lab. and Clin. Med., 1925–26, xi, 186. A Substitute for the Rubber Bulb for Use in the Kolls and Erlanger Blood Pressure Instruments.
5. Stewart, H. J., Proc. Soc. Exper. Biol. and Med., 1924, xxi, 378. A Method for Obtaining Samples of Mixed Venous Blood in Intact Dogs.
6. Stewart, H. J., J. Biol. Chem., 1925, lxii, 641. The Oxygen and Carbon Dioxide Contents of the Arterial and Mixed Venous Blood in Normal Intact Dogs.
7. Van Slyke, D. D., and Neill, J. M., J. Biol. Chem., 1924, lxi, 523. The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement. I.
8. Stewart, H. J., and Gilchrist, A. R., J. Clin. Invest., 1928, v, 335. Studies of the Effect of Cardiac Irregularity on the Circulation. II. The Estimation of Cardiac Output in Dogs Subject to Artificial Auricular Fibrillation.
9. Stewart, H. J., and Crawford, J. H., J. Clin. Invest., 1927, iii, 483. The Effect of Regular and Irregular Tachycardias on the Size of the Heart.