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THE PULSE FLOW IN THE BRACHIAL ARTERY

V. THE INFLUENCE OF CERTAIN DRUGS *

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GENERAL CONSIDERATIONS

By methods which have been described elsewhere¹ we are able to determine (*a*) the average blood flow in the arm of man over brief periods of time, (*b*) the volume and form of the pulse wave entering the arm, and (*c*) the blood flow in the main arm arteries during each portion of the pulse cycle. The last, which we have called the pulse flow in the brachial artery, may be recorded directly. It is, however, a resultant of the two preceding components; that is, of the average blood flow and of the variations in this flow produced by the entrance of the pulse wave into the arm.

The average rate of blood flow in the arm depends in part on the average blood pressure, and in part on the local resistance opposed to the flow of blood through the smaller arteries and capillaries of the arm. By the method which we have used this average blood flow varies considerably even in a single individual, apparently because the body temperature is being constantly regulated by alterations in the rate of blood flow through its peripheral tissues. Even when we have made some effort to maintain a relatively constant external temperature we have at times encountered gradual changes in the rate of arm circulation. For this reason we have not been able to draw conclusions as to the effect of drugs on this rate unless the changes observed were marked and constant.²

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1. Hewlett, A. W., and van Zwaluwenburg, J. G.: The Pulse Flow in the Brachial Artery. I. Technic and General Considerations, *THE ARCHIVES INT. MED.*, 1913, **12**, 1.

2. G. N. Stewart (Studies on the Circulation in Man. I. The Measurement of the Blood Flow in the Hands, Heart, 1911, **3**, 33) found, on the contrary, a rather constant rate of blood flow through the hand for any given individual. In the method which he used the hand is immersed in water of a relatively constant temperature. Possibly this may exercise a steadying influence on the local blood flow.

The volume and form of the pulse wave entering the arm depend on a complex interaction of many factors. Among these are the size and duration of the ventricular output and the condition of the large and small arteries, not only in the arm itself, but in important vascular areas elsewhere. An adequate physical explanation of changes in the volume and form of the pulse does not seem possible at the present time. In the present paper, therefore, I propose merely to record some observations in which the pulse flow in the arm was determined before and after the administration of certain drugs in therapeutic doses.

Nitroglycerin.—The changes which follow the placing of one or two drops of a 1 per cent. solution of nitroglycerin on the tongue have been described in a previous paper.³ These consist of: (1) a swelling of the arm; (2) an increase in the size of the volume pulse; (3) a change toward a more pointed or collapsing pulse; (4) the disappearance of the smaller secondary waves, and (5) no marked or constant alteration in the rate of blood flow through the arm. These typical pulse changes usually begin in two or three minutes, reach their maximum in five or six minutes and pass off in about fifteen minutes. A considerable number of observations, fifty or more, have shown the constancy of these changes in normal young adults. In chronic arterial hypertension, similar changes may also be produced, although not so readily as in young adults. It is noteworthy that the pulse changes in such patients may occur, even when the blood pressure, though reduced, is still far above the normal.

Inasmuch as it seemed probable that these changes might be due in part to a reduction in the elastic coefficient of the larger arm arteries, and that such a reduction might be accompanied by a slower propagation of the arterial pulse wave in the arm, the difference in time between the onset of the subclavian and radial pulses before and during the typical nitroglycerin action was determined in eleven experiments. In four of these the propagation of the pulse wave became somewhat slower, while in the remaining seven no definite alteration in the rate of propagation could be demonstrated. It seems evident, therefore, that the typical changes in the pulse may occur without a demonstrable alteration in the rate of pulse propagation from the neck to the wrist.

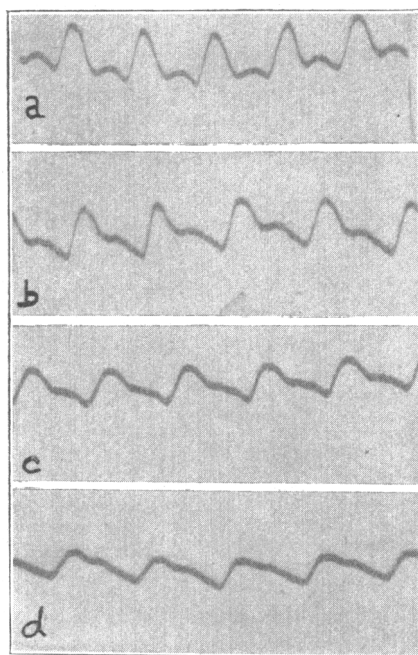
In a previous paper³ it was pointed out that the changes induced by nitroglycerin are more evident in the volume pulse of the arm than in the pulse recorded by placing a tambour over the carotid or sub-

3. Hewlett, A. W., van Zwaluwenburg, J. G., and Agnew, J. H.: The Pulse Flow in the Brachial Artery. II. Relation to the Average Blood Flow. Effect of Nitroglycerin, *THE ARCHIVES INT. MED.*, 1913, **12**, 13.

clavian arteries. Changes in the latter do occur, however, and subsequent records have shown that in some instances they are quite striking. One must therefore attribute the alteration in the arm pulse not only to local vascular changes, but also, in part, either to an alteration in the cardiac output or to changes in the vessels elsewhere in the body.

Electrocardiograms were made on several occasions before and during the nitroglycerin effect, but no noteworthy changes in form were noted.

Pituitary Extract.—It is well known that injections into animals of extracts prepared from the posterior lobe or from the pars intermedia



Curves showing alterations in the febrile pulse produced by the injection of 1.5 c.c. of pituitary extract (from Patient 2 (Sw.) of Table 1). *a.* Before the injection; *b.* seventeen minutes after the injection; *c.* twenty-two minutes after the injection; *d.* fifty minutes after the injection. Note that the volume pulse diminished in size and that its form changed from the pointed or collapsing type, often seen in fevers, to a sustained type.

of the pituitary gland, produce an arterial constriction with a rise of blood pressure. The effect of therapeutic doses on the blood pressure of certain patients was studied in this clinic by Dr. H. B. Schmidt, who found that while the systolic pressure was not altered in any constant manner, there was, as a rule, a moderate rise in the diastolic pressure.

TABLE 1.—EFFECT OF PITUITARY EXTRACT ON PULSE FORM IN PATIENTS SHOWING A POINTED TYPE OF PULSE

Case	Diagnosis	Time with Reference to Pit. Extr.	Pulse Rate	Volume of Pulse Wave, c.c.	Blood Flow in Arm	Pointed Quality
1. Sw.	Tuberculosis	Before	118	0.8	++++
		Before	113	0.7	++++
		Before	109	0.8	++++
		Before	108	0.7	++++
		5 min. after	118	0.6	++++
		1.5 c.c.				
		10 min.	114	0.6	++++
		18 min.	107	0.6	++++
		30 min.	98	0.5	+
		38 min.	97	0.5	+
2. Sw.	Tuberculosis	Before	108	0.33	++++
		Before	112	0.34	1.6	++++
		2 min. after	100	0.37	2.4	++++
		1.5 c.c.				
		4 min.	90	0.33	1.9	++
		6 min.	96	0.33	1.9	++++
		8 min.	104	0.33	1.7	++++
		13 min.	140	0.46	12.0	++++
		15 min.	111	0.30	4.3	++++
		17 min.	106	0.29	1.9	+
		22 min.	104	0.26	2.7	+
		25 min.	96	0.26	2.0	—
		35 min.	96	0.26	1.9	—
		40 min.	95	0.26	2.4	—
		50 min.	92	0.24	2.2	—
3. O. H.	Tuberculosis	Before	75	0.5	3.0	+++
		Before	80	0.5	2.5	+++
		3 min. after	73	0.45	2.6	+++
		1.5 c.c.				
		8 min.	74	0.45	2.5	+++
		10 min.	77	0.4	4.5	+++
		11 min.	73	0.45	4.5	++
		15 min.	76	0.45	2.0	++
		20 min.	80	0.45	2.4	+
		25 min.	80	0.4	2.8	+
		30 min.	82	0.4	+
		35 min.	75	0.35	2.4	—
		40 min.	74	0.3	+
		50 min.	75	0.3	1.2	—
		55 min.	70	0.3	2.0	—
4. C.	Fever	Before	117	0.5	4.0	+++
		Before	117	0.45	3.4	+++
		3 min. after		0.43	3.0	++
		1.5 c.c.	115			
		6 min.	115	0.35	3.0	+
		9 min.	117	0.4	5.0	—
		14 min.	119	0.4	6.0	—
		22 min.	112	0.4	—
		32 min.	120	0.35	6.7	—
5. K.	Fever	Before	65	0.5	++
		Before	66	0.5	++
		14 min. after	66	0.45	+
		1.5 c.c.				
		16 min.	64	0.4	+
		20 min.	70	0.35	—
6. H.	Tuberculosis	Before	98	0.6	7.5	+++
		Before	100	0.6	7.5	+++
		Before	102	0.6	6.5	+++
		3 min. after	100	0.6	6.8	++
		1.5 c.c.				
		7 min.	98	0.6	8.0	+++
		10 min.	97	0.6	8.0	++
		14 min.	102	0.6	9.0	++
		32 min.	103	0.5	7.3	++
		34 min.	104	0.6	9.0	++
		42 min.	97	0.5	7.2	++
		55 min.	100	0.5	7.0	++
7. A.	Tuberculosis	Before	122	0.4	2.0	++++
		Before	121	0.4	1.9	++++
		5 min. after	117	0.4	2.0	++++
		1 c.c.				
		10 min.	115	0.4	2.0	++++
		20 min.	117	0.4	2.4	++++
		30 min.	117	0.4	3.0	++++
8. L.	Aortic insufficiency	Before	88	1.5	5.0	+++
		Before	94	1.4	+++
		5 min. after	84	1.3	++
		1 c.c.				
		7 min.	85	1.3	4.0	++
		10 min.	84	1.3	10.0	+
		17 min.	87	1.2	12.0	+
		22 min.	88	1.3	8.0	++

We have shown elsewhere⁴ that in many fevers, and particularly in typhoid fever and in febrile tuberculosis, the pulse form resembles that produced by nitroglycerin, but that its size is on the average smaller than normal. We have gained the impression, furthermore, that as the circulation shows evidence of failure during infections, the pulse becomes progressively smaller. The effect of pituitary extracts on this type of pulse was studied with the hope that some basis might be furnished for the use of such extracts during the circulatory failure which may complicate severe infections.

The effects that were observed after the intramuscular injection of pituitary extract⁵ are shown in Table 1 and in Figure 1. When striking changes occurred they consisted of: (1) a decrease in the size of the volume pulse; (2) a change from a pointed to a more sustained pulse, and (3) some tendency for a transient increase in the blood flow through the arm, which increase was not definitely related to the change in pulse form and volume. The alterations in pulse volume and form usually became evident in from five to ten minutes after the injection of the pituitary extract, and they persisted for thirty to fifty minutes or more. The onset and duration of this action on the pulse corresponds to the onset and duration of the effects on uterine contractions during labor, for Quigley⁶ asserts that these latter appear in three to ten minutes and last from sixty to ninety minutes.

In six of the eight observations here recorded the changes in the pulse produced by the pituitary extract were marked; in one they were indicated, while in one, in which 1 c.c. only was injected, they were absent. A considerable number of other pituitary extract injections were given without making a series of records. In some of these the above effects on the pulse were confirmed by a few records, while in still others the change to a smaller and more sustained radial pulse was noted on palpation of the radial artery. The carotid or subclavian pulse was recorded in a few instances and a similar tendency toward a more sustained form under the influence of pituitary substance was noted.

It seems certain, therefore, that pituitary extract in rather large doses produces a definite and fairly constant alteration in the size and form of the volume pulse recorded from the arm of febrile patients. This alteration is almost the opposite of that produced by nitroglycerin.

4. Hewlett, A. W.: The Pulse Flow in the Brachial Artery. IV. Reflections of the Primary Wave in Dicrotic and Monocrotic Pulse Forms, *THE ARCHIVES INT. MED.*, 1914, **15**, 609.

5. The preparation of Parke, Davis & Co. (puitritin) was injected intramuscularly, usually in doses of 1.5 c.c.

6. Quigley, J. K.: Pituitrin in Obstetrics, *New York State Med. Jour.*, 1913, **13**, 317.

On account of this contrast, as well as on account of the known effect of pituitary extracts on animals, it seems highly probable that the changes observed in patients were due to arterial constriction. In our opinion, however, such a constriction is not likely to prove of great value in combating the circulatory failure during infections. In the first place, the volume pulse is usually quite small during such collapse, and pituitary extract, though restoring the normal form, makes the volume still smaller. In the second place, it seems probable that this type of circulatory failure is not due primarily to arterial relaxation, but to a deficient blood supply to the heart, owing perhaps to a stagnation of blood in the abdominal capillaries and veins. We have no evidence that pituitary extract will influence such a disturbance in the blood supply to the heart.

Veratrum Viride.—The effect of veratrum album on the pulse rate and the blood pressure of man has been recently studied by Collins,⁷ who found that large therapeutic doses reduce both the pulse rate and the blood pressure, and that these reductions may occur in certain cases without unpleasant gastro-intestinal symptoms. We have repeated these observations, using the hospital tincture or the fluid extract of veratrum viride, and were able to confirm Collins' observations. The effective dose, however, was considerably larger than that used by Collins, and it is evident that some method of standardization will be necessary if veratrum is to be employed in general practice.

Like Collins, we found that in some patients with chronic arterial hypertension, extraordinary reductions of the blood pressure can be produced by this drug. In one patient, for example, the systolic pressure fell from over 200 to 108 mm. in the course of a few hours. Other patients with normal as well as with increased blood pressure proved more resistant to the drug, and in one instance vomiting occurred at a time when no reduction of blood pressure had taken place. It is noteworthy, however, that the reduction in blood pressure may occur with none of the disagreeable symptoms which usually accompany a similar reduction after large doses of the nitrites. In several patients with chronic hypertension the tincture of veratrum viride was continued for several days in doses of 30 or more minims three or four times a day with no unpleasant symptoms, and with a slight but not very definite reduction in pressure.

In eight instances the pulse flow in the arm was recorded before and during the administration of veratrum viride. These records (Table 2) show that the fall in blood pressure produced by this drug is not accompanied by the changes in pulse size or form which char-

7. Collins, R. J.: The Clinical Actions of Veratrum, THE ARCHIVES INT. MED., 1915, **16**, 54.

acterize the action of effective doses of nitroglycerin. It will be recalled that the latter cause an increase in the size of the volume pulse in the arm and that they tend to produce a pointed pulse. When veratrum viride is given in effective doses there may be a slight increase in the volume of the individual pulse waves, but this is not constant; nor is the form of the pulse wave materially altered. When changes in

TABLE 2.—EFFECTS OF VERATRUM VIRIDE

Case	Dose of Tincture, Minims	Blood Pressure	Pulse Rate	Volume of Pulse Wave, c.c.	Blood Flow in Arm	Pointed Quality
1. Kn.	Before	242-140	78	0.45	0.86	++
	After 90	210-122	60	0.52	1.0	+
2. Sm.	Before	166-106	92	0.42	1.7	—
	After 160	130-60	74	0.60	1.7	—
	Followed by Atropin 1/60 gr.	130-88	90	0.37	2.1	+
3. Sm.	Before	200-126	102	0.60	—
	After 120	122-70	70	0.58	Increased	—
4. Ja.	Before	112	0.76	++
	After	95	0.70	++
5. Ja.	Before	126-72	96	0.60	+
	After 140	126-70	96	0.78	+
6. McG.	Before	186-105	99	1.08	—
	After 200	183-110	100	1.2	++
7. In.	Before	260-132	84	+
	After	186-100	60	+
8. Ga.	Before	220-112	87	1.3	++
	After	204-103	60	1.3	Increased	—

TABLE 3.—EFFECT OF ATROPIN ON ARM PULSE *

No.	Time	Pulse Rate	Volume of Pulse Wave, c.c.	Blood Flow in Arm	Pointed Quality
1	After	66	0.4	4.0	—
	Before	73	0.3	3.5	+
2	Before	75	0.3	1.3	++
	After	85	0.3	1.7	++
3	Before	61	0.6	1.7	+
	After	82	0.5	3.4	++
4	Before	76	0.4	1.4	—
	After	80	0.5	2.0	—
5	Before	60	0.7	—
	After	62	0.6	Increased	—
6	Before	100	0.3	2.0	++
	After	140	0.4	3.8	++++

* Records taken before and about half an hour after the injection of 1/50 gr. atropin sulphate.

form did occur, the collapsing quality was more frequently lessened than increased. These slight alterations in the direction of a larger and more sustained pulse may in all probability be attributed to the slower pulse rate rather than to any change in the arteries.

Atropin.—On six occasions atropin sulphate was injected subcutaneously in doses of $\frac{1}{50}$ grain, and the effect on the pulse flow was

recorded at the end of about half an hour. The subjects of these observations were normal so far as the cardiovascular apparatus was concerned. As may be seen from Table 3, the pulse rate was somewhat accelerated in four instances, considerably accelerated in one, and unaffected in one. The size of the volume pulse in the arm was not materially altered. The rate of blood flow was somewhat accelerated in five instances and diminished in one. The pulse form became slightly more pointed in four instances, and it is noteworthy that this change occurred in those cases which showed the more marked acceleration in the pulse rate.

Negative Results.—Records made after the injection of a number of other remedies which are believed to act on the cardiovascular apparatus showed no definite or marked effect on the pulse flow.

In seven patients the pulse flow was determined before and after the intravenous injection of strophanthin. In six patients who had a normal sinus rhythm, no striking changes were observed. Two of these had the typical pointed pulse of fever, while two others were suffering from mild grades of cardiac decompensation. The seventh patient, who showed auricular fibrillation and a rapid and irregular pulse, reacted with the usual slowing of the ventricular rate. This was accompanied by an increase in the size of the individual pulse waves.

Camphor dissolved in oil, in doses of from 5 to 10 grains, was injected subcutaneously into five patients, three of whom showed a pointed febrile pulse. No noteworthy alterations either in the pulse size or form were noted.

Pulse records were made in two patients who received subcutaneous injections of epinephrin solution for the relief of asthmatic attacks. One received 8 and the other 15 minims of Parke, Davis and Company's 1 to 1,000 solution. Although the paroxysms of asthma were relieved, no effect on the pulse form was observed.

Finally, a number of injections of strychnin sulphate were given in doses of $\frac{1}{20}$ to $\frac{1}{10}$ grain without any definite effect on the size or form of the pulse waves. In some of these cases, however, there appeared to be an increase in the rate of blood flow in the arm, which became most evident about half an hour after the injection.

CONCLUSIONS

Of the drugs studied, nitroglycerin, pituitary extract, veratrum viride, atropin, strophanthin, camphor, epinephrin and strychnin, only the first two produced definite and unmistakable alterations in the size and form of the volume pulse recorded from the arm of man. Nitro-

glycerin caused the pulse to become larger and more pointed, while pituitary extract had the opposite effect.

The fall of pressure produced by adequate doses of *veratrum viride* is not accompanied by definite changes in the pulse form. In this respect the action of this drug differs essentially from the action of nitroglycerin.

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