

In functional pathology, nephritis today presents the aspect of a threefold problem: the problem of edema, the problem of uremia, and the problem of hypertension. The first is well on the road to solution, and in practical therapeutics has lost most of its difficulties. Of the second we have barely scratched the surface. The third, seventy-five years after the first clear statement made by Bright, still baffles our best attempts at solution. That it will yield up its secrets through the increasing application of exact physiologic methods at the bedside and through the discovery of means for reproducing the lesions of chronic nephritis in animals, I confidently believe. Then, and not until then, may we hope for the final merging of morphology and physiology in a higher synthesis. The finished picture of nephritis will appear the same from either aspect; all specialization of function basing itself upon known differentiation of structure, and every alteration of structure manifesting itself by intelligible disturbance of function. It is the task of clinical medicine to effect this final reconciliation, for only the clinician must at all times look at disease from both points of view. In accuracy of observation and refinement of technique the medicine of that day may surpass ours by far more than our laboratories surpass the meagre equipment of Guy's of seventy-five years ago; but the method will still be the method of Richard Bright, the careful comparison of the symptoms studied during life with the lesions found after death.

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### THE CIRCULATION IN THE ARM OF MAN.<sup>1</sup>

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THE circulation in an organ, though dependent primarily upon central conditions, such as the cardiac output and the pressure in the larger veins and arteries, is markedly influenced by the condition of the local bloodvessels. These mainly determine the local blood flow, they regulate the amount of blood held in the organ, and they modify the character of the local arterial pulsations. Few parts of the human body are sufficiently accessible for a study of the local circulation by satisfactory bloodless methods. To this rule, however, the extremities constitute an exception. The arm especially has long been an object of circulatory studies, and within recent years various refinements in older methods and the addition of several new methods have added materially to our

<sup>1</sup> Read at the Cleveland Academy of Medicine, November 15, 1912

knowledge of the circulation in this limb. While the accuracy of the methods available on man is not in general equal to the accuracy of the bloody methods employed on animals, nevertheless the results obtained on man are of peculiar interest. In the first place the radial pulse is so frequently examined by physicians that a broader scientific knowledge of the conditions which may affect this pulse is desirable. Again, the effect which psychic processes exert upon the circulation in a limb can be investigated far better in man than in animals. Finally, many pathological processes can be studied only as they occur naturally in man, and we must turn to patients therefore for a better understanding of these processes and of the effect of treatment upon them.

**METHODS.** The record of simple volume changes by means of the plethysmograph has been for years our most important method for studying local variations in the arm circulation. Although this method of study has contributed much to our knowledge even within the last few years, nevertheless plethysmograph records suffer from certain inherent defects. For example, they record changes in the arm volume without telling us anything about the circulation at the beginning of an experiment. Furthermore, changes in volume may be due to changes in the caliber of either arteries, capillaries, or veins; and constant and definite relations do not exist between such volume changes and the local blood flow.<sup>2</sup>

Veiel<sup>3</sup> has recently restudied the radial pulse. For this purpose he used the mirror recorders of O. Frank, which follow the details of the curves with great precision. Space will not permit a review of this work, but I will mention in passing that these and similar studies<sup>4</sup> have shown that the finer details of the radial pulse and even of the brachial pulse, differ greatly from those of the aortic and the carotid pulses. They are in fact peripheral pulses, and their form depends largely upon the condition of the local arteries. We<sup>5</sup> are now engaged in a study of the volume pulse of the arm and of the flow pulse in the brachial artery by means of the mirror recorders of Frank. The volume pulse of the arm, obtained from a plethysmograph, records the difference between the varying entrance of arterial blood and the constant or nearly constant exit of venous blood. If, for example, 2 c.c. of blood enters the plethysmograph by way of the artery with the primary pulse wave and at the same time  $\frac{1}{4}$  c.c. leaves by way of the veins, then the swelling which is recorded as the volume pulse would amount to  $1\frac{3}{4}$  c.c.

<sup>2</sup> V. E. Henderson, and O. Loewi, Ueber die Wirkung der Vasomotorenreizung, Arch. f. exp. Path. u. Pharm., 1905, lili, 56.

<sup>3</sup> Ueber die Bedeutung der Pulsform, Deut. Arch. f. klin. Med., 1912, cv, 249.

<sup>4</sup> O. Müller and E. Weiss, Ueber die Topographie, die Entstehung, und die Bedeutung des menschlichen Sphygmogrammes, Deut. Arch. f. klin. Med., 1912, cv, 320.

<sup>5</sup> A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, Trans. Assoc. Amer. Phys., 1912.

If the veins are momentarily obstructed, or if the normal venous outflow is known, then the volume pulse becomes (or can be translated into) a record of the arterial inflow at each point of the pulse cycle. We shall speak of this as the flow pulse of the brachial artery, for most of the blood enters the portion of arm studied through this channel.

The tachograph of von Kries<sup>6</sup> attempts to record the variations in the velocity of the arterial blood stream to the arm, but it does not record the constant upon which these variations are superimposed.<sup>7</sup> Similar velocity curves may be derived by the method of Fick<sup>8</sup> from volume curves, and with present methods they should be more perfect technically.

Two methods for estimating the blood flow in the arm or hand of man have been recently described. The first of these, which we have mostly used is based upon a principle described by Brodie and Russell,<sup>9</sup> and will be spoken of as the plethysmographic method.<sup>10</sup> The patient lies in a reclining or semi-reclining position and the slightly elevated arm is placed in a plethysmograph, which is connected with a volume recorder. A narrow pressure cuff, similar to that used for determining blood pressure, is then placed about the arm, just outside of the plethysmograph. While the volume of the arm is being recorded the pressure in the cuff is suddenly raised to about the diastolic arterial pressure by opening a valve that places the cuff in communication with a large bottle containing air under pressure. The pressure in the cuff obstructs the veins, but leaves the arteries open. For a short time therefore the blood flows freely into the arm, but cannot escape. At this time the swelling of the arm, as indicated by the volume recorder, corresponds to the normal rate of arterial inflow. Naturally only the first portion of such a record can be used: (1) because the inflow is soon obstructed by the collection of blood in the veins and capillaries, and (2) because the rising venous pressure will eventually force blood beneath the obstructing cuff. The operation of these factors causes a gradual lessening in the rate of arm swelling, which is apparent on the tracings. The longer the period of a constant rate of swelling the greater the reliance that one may place on the accuracy of a given record. In order to increase the reservoir in which blood may collect without raising the pres-

<sup>6</sup> Studien zur Pulslehre, Freiburg, 1892.

<sup>7</sup> J. von Kries, Ueber die Methoden zur Beobachtung der arteriellen Blutströmung beim Menschen, Zeitschr. f. exp. Path. u. Thorap., 1911, ix, 453; Christen, Tachogramm, Pulsvolumen, und Schlagvolumen, Zeitschr. f. exp. Path. u. Thorap., 1911, ix, 607.

<sup>8</sup> Gesammelte Schriften, Würzburg, 1904, iii, 550.

<sup>9</sup> On the Determination of the Rate of Blood Flow Through an Organ, Jour. Phys., 1905, xxxii, p. xlvii.

<sup>10</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, The Rate of Blood Flow in the Arm, Heart, 1909, i, 87. (The use of "we," etc., throughout this paper refers to work done by the author, either alone or in collaboration with other members of the staff in the Department of Internal Medicine, University of Michigan.)

sure in the vessels, a slight elevation of the arm, which tends to empty the veins, is of considerable technical importance.

The second method for determining the blood flow in the hand is that described by G. N. Stewart.<sup>11</sup> As it involves a measurement of the amount of heat given off from the hand in a calorimeter, it will be referred to as the calorimetric method. This method depends upon the principle that the heat thus given off is derived almost entirely from the blood that circulates through the hand. Knowing (1) the amount of heat given off from the hand, and (2) the temperature of the blood which enters and that which leaves the hand, one may calculate how much blood may have passed through in order to give off the heat eliminated.

**PSYCHIC EFFECTS.** Over thirty years ago, A. Mosso<sup>12</sup> showed that increased attention and mental work caused a diminution in the volume of the arm and in the size of the volume pulse. These observations have since been confirmed and extended by numerous investigators,<sup>13</sup> and the relation of these volume changes to those occurring in other parts of the body, as well as their relation to the different types of psychic stimuli, have been repeatedly studied. According to Weber the following changes in the distribution of blood in the body occur as a result of mental or emotional activity.

WEBER'S TABLE.

	Brain.	External head.	Abdominal organs.	Limbs and external trunk.
An impulse to motion with or without execution of the movement . . .	+	-	-	+
Mental work . . . . .	+	-	+	-
Terror (surprise) . . . . .	+	-	+	-
Pleasure . . . . .	+	+	-	+
Unpleasant sensations . . . . .	-	-	+	-
Sleep . . . . .	+	-	-	+

+ indicates an increase and - indicates a diminution in the content of blood in the part.

It will be seen that most emotional and mental processes, with the exception of pleasurable sensations, are associated with temporary decreases in the arm volume. These changes are accompanied by changes of a similar character in all the extremities and in the surface of the trunk and by changes of an opposite character in the volume of the abdominal organs—a reciprocal relation which is rather general, and is known as the Dastre-Morat Law. The above changes in arm volume are usually associated with corresponding changes in the size of the volume pulse.

<sup>11</sup> The Measurement of the Blood Flow in the Hands, Heart, 1911, iii, 33.

<sup>12</sup> Die Diagnostik des Pulses, Leipzig, 1879.

<sup>13</sup> A. Lehmann, Elemente der Psychodynamik, Leipzig, 1905. E. Weber, Der Einfluss psychischer Vorgänge auf den Körper, Berlin, 1910.

These psychic vasomotor changes also affect the blood flow through the arm. When the subject's attention or interest was aroused we have repeatedly observed a sudden reduction in blood flow, which might amount to 30 per cent. or more; and such sudden changes have occasionally proved confusing when the effect of other factors upon the blood flow in the arm was being studied. These sudden changes in blood flow are particularly marked in young and neurotic individuals.

**EFFECT OF EXERCISE.** Since the experiments of Chauveau and Kaufmann<sup>14</sup> on the horse it has been known that the voluntary use of muscle is associated with a marked acceleration of the local blood flow, the increase in the experiments of these investigators being from four to nine times the resting flow. Volume changes in the arm of man during local exercise are difficult to measure by the plethysmograph, because the exercise disturbs the tracings; but direct measurements of the arm volume before and after exercise show increases in volume, which may amount to 200 c.c.<sup>15</sup> The rate of the blood flow in the arm of man is certainly markedly increased, for we<sup>16</sup> found the flow from three to eight times the normal immediately following local exercise, and Stewart obtained a definite increase for the hand in one experiment.<sup>17</sup>

Muscular contractions produced in animals by stimulation of the local nerves seem to be much less effective in accelerating the local blood flow.<sup>18</sup> Massage causes no arm swelling.<sup>19</sup> It would seem that the local circulatory changes are due only in small part to the mechanical effect of the muscular contractions; in the main they are due to vasomotor effects associated with the normal voluntary innervation of the muscles sent out from the higher nerve centres, for Weber<sup>20</sup> has shown that marked swelling of the arm may be induced in a motionless person during hypnotic sleep merely by the suggestion of motion in this arm.

Exercise of one arm has but little effect upon the blood flow in the other motionless arm. We have<sup>21</sup> found no change or a slight increase, and Stewart<sup>22</sup> found a moderate diminution. In Weber's experiments during hypnosis the volume of the opposite arm changed but slightly—sometimes in one direction and sometimes in the other. Vigorous exercise, with rise of blood pressure

<sup>14</sup> Compt. rend. de l'acad. des sciences, 1857, civ, 1126.

<sup>15</sup> Rancken, Ueber die Volumenverhältnisse des Armes bei Massage, aktiver Muskelarbeit und lokalem Heissluftbade, Skan. Arch. f. Physiol., 1910, xxiii, 55.

<sup>16</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

<sup>17</sup> O. N. Stewart, loc. cit.

<sup>18</sup> J. A. Tachniewsky, Ueber die Aenderung des Blutstroms im Muskel bei tetanischer Reizung seines Nerven, Arch. f. d. gesamt. Physiol., 1903, xlvii, 289; R. Burton-Opitz, Muscular Contraction and the Venous Blood Flow, Amer. Jour. Physiol., 1903, ix, 161.

<sup>19</sup> Rancken, loc. cit.

<sup>20</sup> Loc. cit.

<sup>21</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

<sup>22</sup> G. N. Stewart, loc. cit.

and warming of the body, will, however, increase the flow in an unused extremity. For example, immediately after violent exercise on the stationary bicycle the blood flow in the arm is considerably increased, but it falls with the fall of blood pressure, and the final level may be but little different from the original. In some individuals, however, the final level is somewhat raised due presumably to the warming effect of exercise.

**THERMIC EFFECTS.** The circulation in the arm is exceedingly sensitive to thermic influences, whether acting upon the local skin surface or upon some distant part of the body. When subjected to heat the arm becomes larger and softer, the skin becomes warm moist, and often reddened, the arteries feel large and soft, and the veins stand out prominently. All methods of study show that when heat is applied to the arm the bloodvessels tend to relax. The swelling of the arm may amount to 70 c.c.,<sup>23</sup> the volume pulse becomes larger,<sup>24</sup> the tachogram higher,<sup>25</sup> the blood flow may be increased from three to eight times the original,<sup>26</sup> and the venous pressure rises. If the application of heat causes pain there may be a temporary constriction of the vessels of the arm, owing to the psychic effect of the pain, following which the usual dilatation occurs. After the arm has been exposed for some time to high temperatures there is a tendency for the vessels to remain dilated and the blood flow rapid, even though the arm is subsequently somewhat cooled. It has been maintained, though to my mind not proven, that a paresis of the vessels exists in such cases.<sup>27</sup> Mild degrees of burn, as indicated by local reddening, which persists for days, are certainly due to a paralytic hyperemia, affecting chiefly the skin capillaries.

When the arm is exposed to local cold it tends to shrink. Gloves and rings fit more loosely, the skin feels cold and is pale or cyanotic, the radial artery is small and hard, the cutaneous veins become smaller or may disappear, the tachogram and volume pulse lessen in size, and the blood flow diminishes to one-fourth of the normal or even less. When the cold is intense and continued for some time the volume of the arm may again increase slightly,<sup>28</sup> and somewhat more heat is said to be given off from the hand at such extreme temperatures.<sup>29</sup> In most persons, however, we have been unable to obtain an increased blood flow during exposures to water sufficiently cold to cause considerable pain. The skin cyanosis and

<sup>23</sup> Rancken, loc. cit.

<sup>24</sup> A. Mosso, loc. cit.

<sup>25</sup> Balli, Ueber den Einfluss lokaler und allgemeiner Erwärmung und Abkühlung der Haut auf das menschliche Flammuntachogramm, Dissertation, Bern, 1896.

<sup>26</sup> A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, The Effect of Some Hydrotherapeutic Procedures upon the Blood Flow in the Arm, Arch. Int. Med., 1911, viii, 591.

<sup>27</sup> Ibid.

<sup>28</sup> U. Mosso, L'action du chaud et du froid sur les vaisseaux sanguins, Arch. ital. de biol., 1889, xii, 346.

<sup>29</sup> Robinson and Stiles, External Temperature and Cutaneous Blood Flow, Amer. Phys. Ed. Rev., May, 1909.

swelling during exposure to cold can be explained as due to dilatation of the cutaneous capillaries and venules with edema without there being necessarily a dilatation of the smaller arterioles which chiefly govern the blood flow.

Changes in the room temperature markedly influence the blood flow in the arm. Variations of 50 per cent. in the flow may be produced by changes in room temperature<sup>20</sup> even when the subject feels subjectively comfortable. The variations produced by chilliness on the one hand to beginning perspiration on the other will cause variations in the flow through the arm that may amount to seven to ten times. The relation of these changes in the flow to the flow pulse of the brachial is interesting and instructive. Ordinarily most of the blood enters the arm through the brachial artery during the primary systolic pulse wave, and but little enters during the remaining portion of the pulse cycle. In a set of experiments on a normal individual<sup>21</sup> it was found that during exposure to a cold room the primary pulse wave was diminished about proportionally to the diminished flow, and that the main entrance of blood still occurred during the primary systolic wave. Approximately the same relation held during warming of the room up to moderately increased rates of blood flow. When the flow became very rapid, however, the size of the primary wave did not increase. At this time a continued rapid flow occurred throughout the entire pulse cycle. Apparently the large arteries had reached a maximum size, but the smaller arteries, which mainly govern the flow, had continued to dilate and allowed a rapid continuous stream to pass through them.

Thermic stimuli in addition to producing local changes in the circulation also influence the circulation in distant parts of the body. In general the application of heat or cold to one extremity causes a volume change in the same direction in the other extremities, and a volume change in the opposite direction in the abdominal organs.<sup>22</sup> Stewart<sup>23</sup> has shown that these vasomotor reflexes also affect the blood flow in the hand, and that they may be conveniently studied by plunging one hand in hot or cold water while the flow in the other is being recorded. The application of heat or cold to the interior of the stomach will cause a variation in volume of the extremities in the opposite direction from the effect of heat or cold applications to the skin (Müller<sup>24</sup>). Although the two arms tend to vary in the same direction it is possible when one

<sup>20</sup> A. W. Hewlett, *The Effect of Room Temperature upon the Blood Flow, etc.*, Heart, 1911, ii, 230.

<sup>21</sup> A. W. Hewlett, J. G. Van Zwailenburg, and J. H. Agnew, *loc. cit.*

<sup>22</sup> O. Müller, *Blutverteilung im menschl. Körper unter den Einfluss thermischer Reize*, Deut. Arch. f. klin. Med., 1905, lxxii, 547.

<sup>23</sup> *The Effect of Reflex Vasomotor Excitation on the Blood Flow in the Hand*, Heart, 1911, iii, 70.

<sup>24</sup> *Loc. cit.*

is exposed to cold and the other to heat for the flow to be slow in the former and fast in the latter.

It is evident, therefore, that thermic applications produce marked variations in the circulation in the arm, and that they may do this either through direct action or through distant reflexes. To what extent slight variations in the temperature of the blood may influence the peripheral blood flow through an action on the medullary centres has not been accurately determined for man. We know that in animals such action may occur,<sup>35</sup> and there is suggestive evidence that the temperature of the blood may be an important factor in the normal vasomotor control of man.<sup>36</sup> We have noticed repeatedly that when the body temperature has been somewhat reduced the blood flow through the arm tends to fall under slight provocation even though the local circulation had been fairly good previously.<sup>37</sup> Also, the general experience in hydrotherapeutic institutes has emphasized the importance of preventing heat losses sufficient to lower the body temperature when attempting to get a good reaction following cold procedures.

**OTHER PHYSIOLOGICAL FACTORS.** In addition to the effect of the psychic processes, exercise, and thermic influences it seems to us probable that other physiological factors may influence the blood flow in the arm of man, for in our experience the rate may vary considerably on different days even though the room temperatures are carefully controlled. As yet, however, we do not know the exact nature of these factors.

**THE ARM CIRCULATION IN DIFFERENT INDIVIDUALS.** The blood flow in the arm varies considerably in different individuals. In our first paper<sup>38</sup> we stated that the flow usually lay between 2 c.c. and 4 c.c. of blood flow per 100 c.c. of arm substance per minute. A wider experience, however, has caused us to modify these figures. In our original experiments the subjects were usually stripped to the waist and the room was often somewhat chilly, both of which factors would tend to lessen the flows. At present we regard the usual variations of blood in the arms of normal individuals as from 2 c.c. to 8 c.c. of blood flow per 100 c.c. of arm substance per minute, while for a given individual variations of 50 per cent. are not uncommon. Stewart's figures for the hand varied from 3.5 c.c. to 14 c.c. of blood flow per 100 c.c. of hand substance per minute, while the variations in a given individual were insignificant. We have shown that this difference in rates as obtained by the two methods also holds on a single individual,<sup>39</sup> the calorimetric method

<sup>35</sup> Kahn, Ueber die Erwärmung des Carotidenblutes, *Arch. f. Anat. u. Physiol. Physiol.*: 1904, Abteil. Supplemental Band, p. 81.

<sup>36</sup> R. Stein, *Zeitschr. f. klin. Med.*, 1892, xx, 63.

<sup>37</sup> A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, loc. cit.

<sup>38</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

<sup>39</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, Comparison Between the Blood Flow in the Arm and in the Hand, *Proc. Soc. Exp. Biol. and Med.*, 1911, viii, 111.



usually giving a more rapid blood flow in the hand relative to its volume than does the plethysmograph method for the arm, and we are inclined to attribute these differences to an actual difference in the circulation, the flow in the hand relative to its volume being greater than in the arm.

When we compare pathological individuals under ordinary conditions with these normal standards we usually find that their blood flows in the arm or hand fall within the normal limits of variation. This rule holds for such conditions as severe anemia, hypertension, and heart disease except in the stage of badly broken compensation. Slow rates are associated in general with cold extremities. The slowest that I have encountered was in a patient with dead fingers in whom the flow was 0.7 c.c. of blood flow per 100 c.c. of arm substance per minute. Stewart also found a slow flow in this condition. The most rapid flows are encountered in those with warm extremities, and of these patients with severe types of Graves' disease show the fastest rates. The most rapid rate that we have encountered under ordinary conditions of room temperature was 19 c.c. of blood flow per 100 c.c. of arm substance per minute.

During continuous fever the blood flow in the arm usually lies within the normal limits of variation. To what extent it differs from what would be the usual flow for the individual studied has not been determined: When the temperature is rising during fever the blood flow in the arm is relatively slow,<sup>40</sup> and during a chill the volume pulse becomes decidedly smaller.<sup>41</sup> When the temperature is falling, on the other hand, the flow is relatively fast and the volume pulse is large.

In general the size of the volume pulse in different individuals corresponds fairly well to the rate of blood flow in the arm, the larger the pulse the more rapid the flow, etc. The main entrance of blood into the brachial artery occurs during the primary systolic pulse wave, after which there is little or no flow. We have already pointed out that when an individual is very warm this relation does not hold, for the flow is then increased out of proportion to the increase in the primary wave and the blood enters the arm rapidly throughout all portions of the pulse cycle. This was found to be true also during muscular exercise and in the rapid flows of severe Graves' disease. In aortic insufficiency the opposite condition may hold. The volume pulse in typical cases is unusually large,<sup>42</sup> and following the primary wave an evident back flow throughout the remainder of the pulse cycle is sometimes but not always present. More blood, therefore, may enter the brachial artery during the primary wave than flows through the arm during the whole pulse cycle. This back flow in the brachial is not, however,

<sup>40</sup> A. W. Hewlett, loc. cit.

<sup>41</sup> A. Mosso, loc. cit.

<sup>42</sup> A. W. Hewlett and J. G. Van Zwaluwenburg, unpublished observations.

characteristic of aortic insufficiency. As we shall see a short wave of backflow is evident in the nitroglycerin pulse, and probably occurs to a lesser extent under other circumstances. It seems possible also to have a slight continuous backflow in other conditions.

**VASCULAR REACTIONS IN DISEASE.** The normal response of the vessels of the arm to psychic and thermic stimuli may be modified during disease. Two methods have been used for studying these abnormal vasomotor reactions. In the first, plethysmographic records are taken while the individual is subjected to some stimulus, such as mental work, pain, or the application of heat or cold to the skin. According to the second the blood flow is determined in one hand while the opposite hand is thrust into hot or cold water.

Weher<sup>43</sup> who has made a special study of psychic processes, found that there was a tendency for the usual vasomotor reflexes associated with attention, and the suggestion of movement to be lessened or even to be reversed during mental or physical fatigue. The reflexes normally produced by pleasant or unpleasant stimuli, on the other hand, were usually unaffected during fatigue. He states also that patients with Graves' disease, neurasthenia, or hysteria often showed such fatigue phenomena more readily than do normal individuals, and that in some of these patients this diminution or reversal of the normal reflexes was constantly present.

The vasoneuroses of which Raynaud's disease may be taken as a type have been studied by Curschmann, Simons, and Stewart. It is generally agreed that such patients usually show abnormal variations in their vasomotor reflexes. As yet, however, there is no general agreement as to character or constancy of these variations. Curschmann<sup>44</sup> found an abolition of the plethysmograph reactions to thermic and to various psychic stimuli. Simons<sup>45</sup> found variable reactions at different times and a lack of symmetry in the reaction on the two arms. Stewart<sup>46</sup> found a transient reaction to cold followed by an increase in the blood flow. It would seem not unlikely that such patients show considerable variations among themselves, and that a given individual may show different reactions at different times.

Organic lesions of the nerves or of the central nervous system may also affect the vasomotor reactions of the extremity. Simons<sup>47</sup> found that the vascular reactions of the hand depended upon an intact condition of the median and ulnar nerves and was inde-

<sup>43</sup> Loc. cit.

<sup>44</sup> Untersuchungen über das funktionelle Verhalten der Gefäße bei trophischen und vasomotorischen Neurosen, Münch. med. Woch., 1907, liv, 2519.

<sup>45</sup> Plethysmographische Untersuchungen der Gefäßreflexe bei Nervenkranken, II, Arch. f. Anat. u. Physiol., Physiol.-Abteil, 1910, Supplemental Band, 429.

<sup>46</sup> Loc. cit.

<sup>47</sup> Plethysmographische Untersuchungen der Gefäßreflexe bei Nervenkranken, I, Arch. f. Anat. u. Physiol., Physiol.-Abteil, 1910, 557.

pendent of the conditions of the radial nerve. Stewart found a transient reaction in patients with neuritis and an abolition of reactions in an old hemiplegic hand.

Arteriosclerosis, as shown by Romberg and his school<sup>43</sup> also tends to abolish the reflexes produced by the application of ice to the upper arm. It is interesting, however, that a thickened radial artery, especially in continuous hypertension, may show a normal or increased reaction. In such cases it may be assumed that the thickening is due to a hypertrophic muscle which shows normal or increased reactive power. In advanced heart disease the vascular reactions may be absent.<sup>44</sup>

**THERAPEUTIC EFFECTS.** Thus far we have accumulated relatively few data concerning the effect of drugs upon the circulation in the arm. It seems certain, however, that the most effective measures at our disposal for influencing this circulation are thermic stimuli applied either locally or to some distant part of the body. Skin irritants, such as mustard, produce a local dilatation of the cutaneous capillaries and venules, but their action upon the blood flow through the part, aside from thermic effects, is relatively slight.<sup>45</sup> One may reconcile these observations by assuming that the chief factor controlling the blood flow is the state of contraction of the small arterioles, and that mustard produces a dilatation of the cutaneous capillaries and venules without a corresponding dilatation of the underlying arterioles.

The intravenous injection of strophanthin<sup>41</sup> or digitalis<sup>42</sup> in therapeutic doses affects neither the volume of the arm nor its normal reaction to the application of cold. Such injections are said, however, to affect the tonus of the larger arteries.<sup>43</sup> Intravenous injections of caffeine diminish the arm volume and intravenous injections of sodium nitrite increase it.<sup>44</sup> We have found that medicinal doses of nitroglycerin dropped on the tongue produce definite changes.<sup>45</sup> Within a few minutes the arm volume increases and the volume pulse becomes larger. The pulsations of the brachial artery as obtained by the Erlanger sphygmomanometer also become larger. The blood flow through the arm is not greatly affected. The flow pulse shows that a large arterial wave enters the arm and that

<sup>43</sup> Romberg and Müller, *Ueber Bedeutung und Technik der plethysmographischen Funktionsprüfung gesunder und kranker Arterien*, *Zeitschr. f. klin. Med.*, 1912, lxxv, 93.

<sup>44</sup> G. N. Stewart, loc. cit.; Romberg and Müller, loc. cit.

<sup>45</sup> C. I. Wood and P. G. Weisman, *The Effect of a Skin Irritant on the Local Blood Flow in the Hand*, *Arch. Int. Med.*, 1912, x, 196.

<sup>46</sup> O. Vogt, *Ueber die Herz und Gefäßwirkung des Strophanthins bei gesunden und kranken Menschen*, *Med. Klinik*, 1909, v, 1853.

<sup>47</sup> H. Eychmüller, *Ueber die Herz und Gefäßwirkung der Digitalis bei gesunden und kranken Menschen*, *Berl. klin. Woch.*, 1909, xvi, 1677.

<sup>48</sup> Nägeli, *Zentralbl. f. Herz. und Krankheiten*, 1910.

<sup>49</sup> O. Müller, *Ueber die Herz und Gefäßwirkung einiger Digitaliskörper bei gesunden und kranken Menschen*, *Verhandl. des Kongr. I. in. Med.*, 1909, xvi, 364.

<sup>50</sup> A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, loc. cit.

it is in large part immediately reflected. We have assumed in such cases a marked relaxation of the larger arteries of the arm, which allows a large pulse wave to enter, while at the same time the finer arterioles are contracted and do not allow the blood to flow through them. Owing in part to the relaxed condition of the large arteries the wave is reflected from the periphery.

**CONCLUSIONS.** In studying the local circulation in the arm of man, local conditions must be kept constantly in mind. The tachogram, the volume pulse, and the finer waves of the radial pulse depend in large part upon the condition of the larger arteries. The blood flow and the temperature of the part depend largely upon the condition of the finer arterioles. The color of the part depends in part upon the condition of the cutaneous capillaries and venules and in part upon the local flow. Changes in any of these cannot be referred unreservedly to changes in the heart action.

Many changes in the local circulation can be referred to thermic effects, and the function of the skin in serving as a physical means of heat regulation must be borne constantly in mind. Conditions of chilliness or warmth, whether occurring as a result of external temperature or as a result of fever, influence most markedly the peripheral circulation in the extremities. If we wish to increase the circulation in an extremity the most effective means at our disposal are general and local warmth. In comparison with these thermic measures the effect of drugs is insignificant.

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### AN INSTANCE OF PREMATURE BEATS ARISING IN THE AURICULOVENTRICULAR BUNDLE OF A YOUNG CHILD.

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E. H., a child, aged four and a half years, has been under observation for eighteen months or more, and whenever examined has shown premature beats of a curious but constant type.

*Family History.* Both parents are living and well. The mother has had at least one attack of rheumatism. Three sisters and brothers are living and well.

*Previous Illness.* As a baby had chickenpox. In November,