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SENSITIVITY OF THE SMALLEST CUTANEOUS BLOOD VESSELS: QUANTITATIVE RESPONSES TO GRADED MECHANICAL STIMULATION AND TO LOCAL ISCHEMIA IN ARTERIAL HYPERTENSION, ARTERIOSCLEROSIS, AND CERTAIN ALLIED DISORDERS¹

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In hypertensive, as well as in normal, subjects, it is generally held that the level of arterial blood pressure is affected largely by the tone of the terminal arterioles; the vessels beyond are only passively concerned (1 to 4). There are, nevertheless, reports to the contrary (5, 6). These studies are, for the most part, based on direct and indirect mensuration of capillary pressure. There is considerable evidence, however, that the smallest blood vessels are involved functionally and morphologically in the disorders of the peripheral vascular tree, in ways other than that which may be demonstrated by the mere determination of the pressure relationship between capillaries and arterioles (7 to 10). The experiments reported here are designed to elucidate this problem by quantification of the responses of the smallest blood vessels in the skin of a selected group of patients, by the use of two methods recently described (11, 12). The first method measures the sensitivity of small dermal blood vessels to graded mechanical stroking (vasoconstriction), while the second measures the hyperemic response consequent to a standardized period of local ischemia (vasodilation). Individual, seasonal, segmental, and aging variations of these responses in normal subjects have been previously described (11 to 13).

METHODS AND PROCEDURES

The management of the patients employed in this study was as follows:² Procedures with any given clinic or ward patient were kept as standardized as possible. After

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² All patients used in these studies were selected from the medical wards and the cardiac clinic, Kings County Hospital, Long Island Medical College division, under the direction of Dr. J. Hamilton Crawford.

a review of the history, a careful physical examination was performed. Especial note was made of any abnormality pointing toward disease of the peripheral vessels. Every patient had a fundoscopic examination, an electrocardiogram, a six foot x-ray plate, blood chemistries, and several urinalyses.

The special determinations of small dermal blood vessel reactivity could usually be done following the physical examination. However, to maintain basal circulatory conditions, the patient rested quietly at least one hour before each determination. In every case, the skin of the ventral surface of the forearms was used as in our previous studies. A strength-duration curve was then determined using a mechanical device capable of varying both the speed and intensity of application of a stroker along the skin. This was done by finding the least weight in grams at each of five critical speeds of the stroker which produced a liminal degree of vasodilation against a background of vasoconstriction. The curve thus obtained was quantitated mathematically using the formula

$$\text{recommended by Lassalle,}^3 E = \frac{1}{\text{Rheobase}^2 \times \text{Chronaxie}}.$$

(For full discussion of this method see (11).) Figure 1 illustrates samples of intensity-duration curves, obtained on three patients with different types of lesions.

The ability of small cutaneous blood vessels to respond by reactive hyperemia to local ischemia was then ascertained. This was done by application of a rubber ring, five square centimeters in area, to the skin of the forearm, the weight loading of which was 100 grams per square centimeter. By varying the length of time in seconds of application of the ring, an area of reactive hyperemia of even intensity, color, texture, and discreteness of edges could be obtained. This was called the *threshold*. By timing the period of time, in seconds, which such a hyperemic area required to fade to the color of the surrounding skin, the *clearing time* was obtained. (For full discussion of this method see (12).) The clearing time has been shown to be directly related to

³ In this investigation, only the Lassalle coefficient will be considered as the significant criterion of comparison of the intensity-duration curves. The rheobase, chronaxie, and the log-log slope of the curves were also analyzed, but it was found that they did not contribute to the clarity of the results.

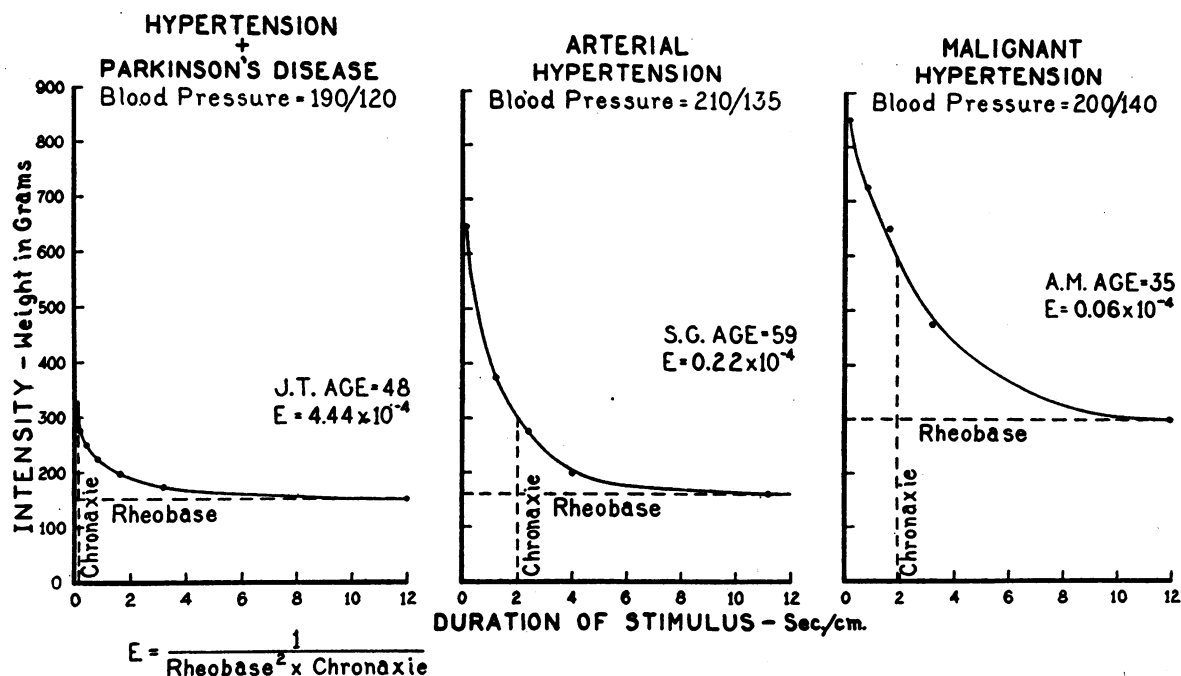


FIG. 1. METHOD OF PLOTTING THE INTENSITY-DURATION CURVES OBTAINED BY MECHANICAL STROKING OF THE SKIN

The Lassalle coefficient, E , is calculated as shown by graphically finding the values of the rheobase and the chronaxie. The three types of patients shown illustrate the range of capillary sensitivity found in this study.

the rate of cutaneous blood flow (12 to 14). Normal values will be discussed later.

No attempt was made to select an especial type of hypertensive patient. All those patients who came to our attention, in the cardiac clinic or on the medical wards, with a diagnosis of arterial hypertension or of arteriosclerosis were accepted for study. These, nat-

urally, included both early and late stages of arterial hypertension and of arteriosclerosis. The sex and age incidence of arterial hypertension of our group of patients agreed very well with that of other investigators (15). Most of the patients were in the sixth decade of life, with a spread of from the third to the eighth decades (see Table I).

TABLE I

Comparison of normal blood vessel reactions with those in arterial hypertension and in arteriosclerosis
Statistical analysis of the data obtained by graded mechanical stroking of the skin (capillary sensitivity).

Type of subject	Number in sample	Mean age	Reactive hyperemia*		Capillary sensitivity					
			Threshold, per cent of normal	Clearing time, per cent of normal	Mean coef. of excitability $\times 10^{-4} \dagger$	Standard deviation \pm	S. E. of the mean \pm	S. E. of difference from the normal mean \pm	t	Probability from Fisher's Table
Normal control	32	53	100	100	0.23	0.332	0.059			
Hypertensive	50	56	104	108	0.24	0.217	0.031	0.0667	0.1498	0.8-0.9
Hypertensive and arteriosclerotic	25	58	95	96	0.21	0.174	0.035	0.0686	0.2915	0.7-0.8
Arteriosclerotic	23	61	105	109	0.18	0.144	0.030	0.0654	0.7645	0.4-0.5
Malignant hypertensive	10	38	See Table II	See Table II	0.08	0.060	0.017	0.0614	2.443	0.02-0.05
Hypertension plus other lesions	13	55	See Table III	See Table III	1.73	1.087	0.301	0.306	4.902	Less than 0.001

* For discussion of the expected normal thresholds of reactive hyperemia in relation to age and season see text.

$\dagger E = \frac{1}{\text{Rheobase}^2 \times \text{Chronaxie}}$

Early in the investigation, it was found that some patients with arterial hypertension also had a considerable degree of arteriosclerosis, and *vice versa*. It was therefore deemed desirable to separate the group into three subgroups, *viz.*, hypertension, hypertension complicated by arteriosclerosis, and arteriosclerosis. The extent of arteriosclerosis was ascertained by the usual clinical methods, *i.e.*, history of coronary occlusion, intermittent claudication, etc., palpation of the radial and superficial temporal arteries, fundoscopic examination, and x-rays of the larger vessels.

For purposes of correlation with the capillary sensitivity test (graded mechanical stimulation), it was necessary to grade arbitrarily the severity of the disease process in the group of patients with uncomplicated arterial hypertension.⁴ This was done by following closely a plan similar to that advocated by Adson and Allen (17). Thus, by consideration of the general symptomatology,

⁴ We feel that it is justifiable to refer to this test as a capillary sensitivity test. The term smallest blood vessels is more strictly proper, for the vessels affected undoubtedly include the finest arterioles and venules, besides the capillaries. However, Lewis (16) clearly presents the reasons why the white and red responses, upon which this test is based, may be considered an index of capillary reactivity.

changes in the retina, and the diastolic and systolic levels of blood pressure, it was possible to divide the patients into four main groups.

To obtain a basis of comparison, the same determinations were done upon a control group in the fifth and sixth decades of life, in which age group, most of our abnormal patients fell. These normals were selected from patients attending the eye clinic for refraction preparatory to the fitting of spectacles. A careful examination was done in each patient to exclude serious disease, especially that involving the cardio-vascular system and the skin.

RESULTS

Sensitivity to graded mechanical stimulation; capillary sensitivity. The results obtained in the normal group may be compared with those in the hypertensive group. By glancing at Table I, it will be seen that the mean coefficient of excitability for the normal group, 0.23×10^{-4} , is very similar to that of the hypertensive group, 0.24×10^{-4} . The coefficients for the hypertensive and arteriosclerotic groups also do not deviate markedly from that obtained in the normal.

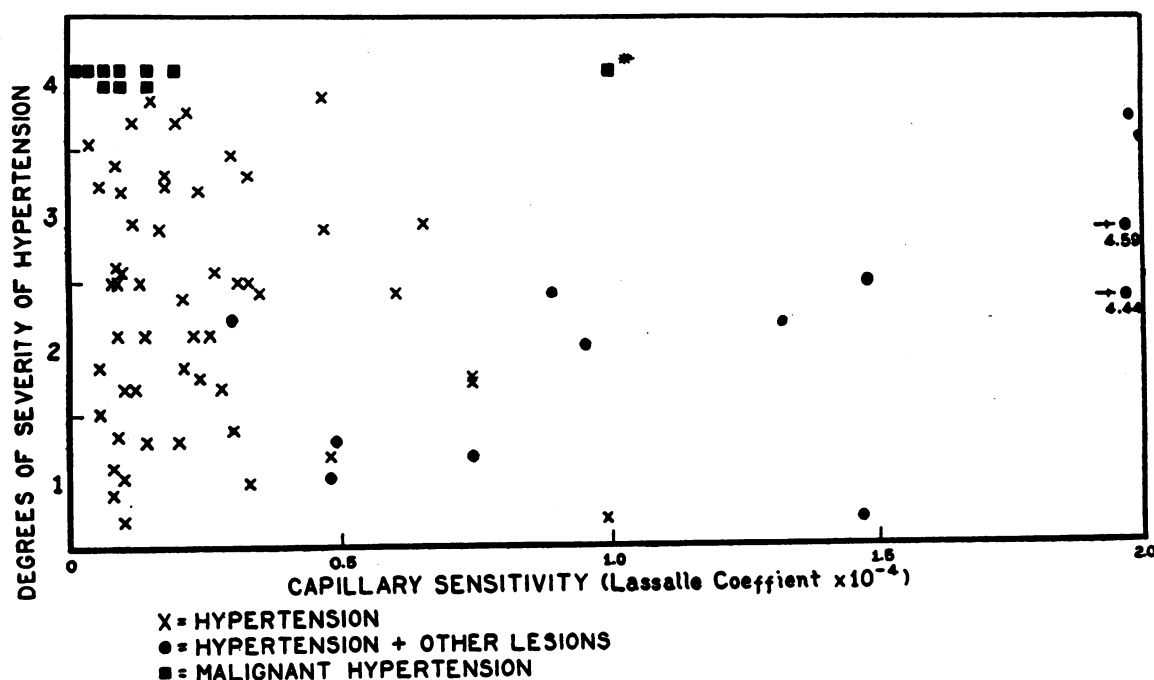


FIG. 2. THE LASSALLE COEFFICIENTS OF THE GROUP OF PATIENTS WITH ARTERIAL HYPERTENSION ARE PLOTTED AGAINST THE SEVERITY OF THEIR DISEASE AS DISCUSSED IN THE TEXT

Scattering of the crosses indicates the lack of correlation. Note that patients with malignant hypertension, and with hypertension associated with other lesions, fall into areas outside the general average of the uncomplicated hypertensives. The solid square marked by the asterisk is the coefficient of a patient who had malignant hypertension complicated by hemiplegia, with residual mental symptoms.

The results of the capillary sensitivity tests in the hypertensive group are graphically illustrated in Figure 2. The individual coefficients (in some cases, the average of as many as four determinations) are plotted against the severity of the hypertensive disease process, arbitrarily ascertained as described above in the section on methods. It is apparent from the scattering of the crosses that capillary sensitivity, as determined by mechanical stimulation of the skin, bears no relationship to the severity of the hypertensive lesions. A number of cases of malignant hypertension, and hypertension associated with certain other lesions, are also charted, which deviate widely from the uncomplicated hypertensive group. These will be discussed below.

Graphs were also plotted (not included in this paper) which permitted interpretation of the influence, if any, of the level of the diastolic and systolic pressure upon the individual coefficients. It was found that the level of either diastolic or systolic pressure had no correlation with the value obtained in the capillary sensitivity test. It is therefore probable that the level of the arterial blood pressure is not a significant factor in the sensitivity of the capillaries, as measured in this study. Furthermore, the capillary sensitivity is not influenced by the degree of severity of the hypertension, except as noted below. These conclusions also apply to the results obtained on patients with hypertension and arteriosclerosis, and with arteriosclerosis alone.

Responses to local ischemia; threshold of reactive hyperemia. The results of the reactive hyperemia test must be considered against the demonstrated normal seasonal variation in this reaction. In a previous study (12), on a large group of normal subjects, it was found that the threshold of reactive hyperemia varied from fifteen to twenty seconds in mid-summer, to seventy to eighty seconds in mid-winter. It was therefore necessary to collect seasonal data on normal subjects simultaneously with that obtained on the hypertensive and arteriosclerotic patients. This was done by weekly determinations on two normal subjects, throughout the course of this study. To this was added from time to time the normal data from other studies then in progress (13, 14). From a seasonal curve, thus constructed, the percentage deviation of the experimental data from

this normal data could be ascertained at any seasonal period throughout the year.

A threshold percentage greater than 100 per cent, or the expected seasonal normal, indicates less ability of the small dermal blood vessels to respond by reactive hyperemia to local ischemia. Similarly, a clearing time percentage greater than 100 per cent denotes a relatively slower cutaneous blood flow. The opposite relationship, obviously, also holds true. Since a scattering of as much as ten per cent may be present in a normal group, such a deviation cannot be considered abnormal in either group of data. It can be seen by glancing at Table I that the thresholds and clearing times of the reactive hyperemia tests do not deviate significantly from the normal, either in the hypertensive or arteriosclerotic groups. It is therefore evident that the small dermal blood vessels are not impaired in their capacity to respond to local ischemia, either in arterial hypertension or in arteriosclerosis. Furthermore, it is possible to infer, from a comparison of the clearing times, that the rate of blood flow in the skin also is not significantly different from the normal, since in previous studies it has been shown that the clearing time is directly related to the rate of blood flow in the skin (12 to 14).

Malignant hypertension. It must not be supposed, however, that the hypertensive process in its most severe phases will not ultimately influence the responses of the smallest dermal blood vessels. Eleven cases of the malignant phase of hypertension came to our attention, eight of whom had distinctly abnormal responses to these tests.⁵ These are summarized in Table II. With the exception of M. S., all had coefficients of excitability which were either normal or distinctly lower than normal. Thus, they ranged from 0.02, the lowest coefficient obtained in the entire series, to 0.20 which was that of the least ill member of the group, as judged by other standards. Patient M. S., who had a coefficient as high as 1.00 on one occasion and 0.38 about three months later, was the only one of the eleven who presented more sensitive dermal blood vessels than the average normal. However, she had a central nerve lesion which may markedly affect these blood vessel re-

⁵ Our viewpoints concerning the nature of malignant hypertension concur closely with those of Derow and Altschule (18).

sponses, as will be discussed later. It is therefore evident that the most severe phases of hypertension may be associated with a considerable decrease in the ability of the small dermal blood vessels to respond to mechanical stimulation.

The responses to local ischemia are even more abnormal. With the exception of R. S., five pa-

tients had a threshold of greater than 200 per cent of normal. Two patients had no reaction at all after five minutes stimulation time, and three patients had incomplete reactions at the end of five minutes stimulation. This is a distinctly abnormal finding, since no normal subject has ever been encountered on whom a response could not

TABLE II
Malignant hypertension

Patient	Sex	Age	Average blood pressure	Capillary sensitivity	Reactive hyperemia		Eye grounds	Urine†	Remarks
				Coefficient of excitability* ×10 ⁻⁴	Threshold, per cent of normal	Clearing time, per cent of normal			
R. S.	F	53	mm. Hg 230/140	0.20	147	100	Exudate; hemorrhage; blurred discs	S.G. = 1021 Alb. = 3+	Excellent skin color
N. C.	F	47	220/110	0.04	300	230	Exudate; hemorrhage	S.G. = 1023 Alb. = 2+	Pale, pigmented skin color
M. S.	F	52	268/180	1.00 0.38	No reaction after 5 minutes		Exudate; extreme spasm of vessels	S.G. = 1026 Alb. = 1+	Hemiplegia with residual paralysis and extreme mental symptoms. Very pale, pigmented skin color
M. V.	F	30	232/156	0.08 0.11	Not complete at 5 minutes		Papilledema; old and fresh hemorrhages	S.G. = 1015 Alb. = 1+	Very pale skin
B. B.	F	52	230/155	0.02	273	137	Exudate; hemorrhage; edema of retina	S.G. = 1015 Alb. = 3+ 4+	Pale, pigmented skin color
M. D.	F	33	260/158	0.05	253	442	Patchy exudate; fresh hemorrhages	S.G. = 1016 Alb. = 1+	Pale, pigmented skin color (Negroid)
A. M.	M	35	200/140	0.06	650	320	Exudate; hemorrhage; blurred discs	S.G. = 1015 Alb. = 2+ 3+	Pale, pigmented skin color
G. P.	M	45	210/132	0.10	No reaction after 10 minutes		Papilledema; old and fresh hemorrhages	S.G. = 1008 Alb. = 2+ 3+	Pale, pigmented skin color
J. W.	M	48	214/150	0.07	303	213	Marked, soft exudate; hemorrhage; spastic closed arteries	S.G. = 1010 Alb. = 2+ 4+	Pale, pigmented skin color. Died 4 days later in uremia
M. L.	M	23	264/148	0.16	Not complete at 5 minutes		Papilledema	S.G. = 1012 Alb. = 4+	Pale, pigmented skin color
M. D.	M	33	210/120	0.15	Not complete at 5 minutes		Blurred discs	S.G. = 1012 Alb. = 2+	Moderately pale skin color

* $E = \frac{1}{\text{Rheobase}^2 \times \text{Chronaxie}}$

† All had abnormal quantities of formed elements in their urine.

TABLE III
Hypertension associated with certain other lesions

Patient	Sex	Age	Average blood pressure	Capillary sensitivity	Reactive hyperemia		Remarks
				Coefficient of excitability $\times 10^{-4} \dagger$	Threshold, per cent of normal	Clearing time, per cent of normal	
A. E.....	F	56	mm. Hg 185/122	1.48	No reaction after 5 minutes		Hemiplegia with residual paralysis and mental symptoms
R. W.....	F	54	146/84	1.47	73	88	Neurasthenia
J. V.....	F	63	140/90	4.59	83	80	3 years ago had high B. P.; after heart attack, had low B. P. Headaches
E. O.....	F	35	140/100	0.95	94	117	Post-encephalitic.
L. A.....	F	68	130/90	0.48	42	45	Parkinson's syndrome
M. M.....	F	39	130/85	0.49	85	81	Parkinson's disease.
M. C.....	F	73	135/85	0.74	49	56	Paralysis agitans
C. W.....	F	50	160/100	0.30	73	56	Post-encephalitic.
J. D.....	M	58	185/120	1.98	170	53	Parkinson's syndrome
J. T.....	M	48	190/120	4.44	93	60	Paralysis agitans
W. K.....	M	77	220/120	1.32	83	120	Parkinson's disease.
M. S.....	M	31	140/100	0.89	77	71	Paralysis agitans
N. M.....	M	49	164/110	2.13	48	141	Post-encephalitic.
							Parkinson's syndrome

$$\dagger E = \frac{1}{\text{Rheobase}^2 \times \text{Chronaxie}}$$

be elicited in ninety seconds with the application of local ischemia, even at the height of the seasonal curve (12). The clearing times in those patients on whom a response could be elicited were as much as 200 per cent greater than normal clearing times, denoting a slowing of cutaneous blood flow. These results, therefore, disclose a marked impairment in the ability of the smallest cutaneous vessels of patients in the malignant phase of hypertension to respond by reactive hyperemia to local ischemia.

The clinical finding of a pale and often pigmented skin in these patients substantiates the dermal blood vessel tests. It is notable that the one patient in the group, R. S., who had normal skin, also had practically normal cutaneous blood vessel reactions (Table II).

Hypertension associated with certain other lesions. Thirteen patients with various types of

nerve lesions, ranging from hemiplegia with residual symptoms to Parkinson's disease, who had abnormal cutaneous blood vessel reactions, were also studied. Thus patient J. T., Table III and Figure 1, had a coefficient of excitability to mechanical stimulation of 4.44, a figure nearly eighteen times that of the mean average for the corresponding group of hypertensives. All the others had coefficients far greater than normal (Table III).

The responses to local ischemia in this group, with the exception of patient A. E. (Table III), substantiate the results of the mechanical stimulation test. Throughout this series, the threshold and clearing times were shorter than the expected normal. This denotes cutaneous vessels more sensitive to local ischemia, and a faster dermal blood flow than in normal skin.

In the light of these findings of increased small dermal blood vessel sensitivity in hypertension with certain associated disorders and especially in central nerve lesions, the high coefficient of case M. S., Table II, a malignant hypertensive, can now be explained. One year previous to admission she had a stroke which resulted in complete hemiplegia, speech defects, and marked disorientation. This, undoubtedly, lead to a coefficient of 1.00 despite her advanced stage of hypertension.

Various other diseases, and especially central nerve lesions, such as hemiplegia and Parkinson's syndrome, greatly increase the responsiveness of small cutaneous blood vessels, both to mechanical stimulation and to local ischemia, even in the face of advanced hypertension. The reasons for this cannot be elucidated in this investigation, however. Further study of this type of patient is necessary.

Statistical treatment. For purposes of analysis, the data were originally separated into male and female groups. No significant differences could be obtained, however, by various tests between these groups. Therefore, the data were combined for presentation in this communication. Moreover, since there were nearly an equal number of males and females in each main group, any differences which might be present neutralized each other.

In order to ascertain further just what significance might be laid on the differences between the mean of the capillary sensitivity tests on the normals as opposed to the experimental groups, the data were treated statistically following the recommendations of Mainland (19). Since, in data of this type, the probability (Fisher's Tables (20)) must be at least 0.05 or less to be significant, it may be seen in Table I that the conclusions which have been placed on the data thus far are correct. Thus the data of the hypertensive, hypertensive and arteriosclerotic, and the arteriosclerotic groups have probabilities of 0.8, 0.7, and 0.4 respectively, putting these data far out of the realm of significance. The malignant hypertensive group has a probability of 0.02 to 0.05, which is just significant. Doubtless, if more of this type of patient could have been studied, the significance would have been greater. The group of hypertensives with associated lesions has a probability of less than 0.001 which may be regarded as highly significant. Therefore one is assured that the dif-

ferences found in the capillary sensitivity tests were real rather than coincidental.

DISCUSSION

It is not surprising to find that the functional responses of the smallest cutaneous blood vessels in various degrees of arterial hypertension, and in arteriosclerosis, are not different from those in normal skin. This is entirely consonant with the viewpoints of others on the dynamics of the circulation in arterial hypertension (1 to 7). The clinical observation that the skin of hypertensive patients shows no signs of atrophy, and presents variations of coloring and texture no different from the skin of normals in the same age range, further substantiates these findings. The observation that the capillaries in the nail fold of arteriosclerotics are often "moth eaten" (21), as seen by use of the capillary microscope, in no way vitiates the conclusion that the small blood vessels of the skin in these patients are not impaired in their functional capacity to respond to mechanical stimulation and to ischemia. There are, no doubt, morphological changes in the smallest vessels with advancing vascular disease, but this does not necessarily imply that their functional reserve to respond to local injury is exceeded (14).

The disclosure of distinctly decreased irritability and impairment of the capacity to respond to local ischemia of the small dermal vessels in the malignant phase of hypertension deserves further consideration. It may be advanced that the extreme narrowing of the arterioles in this condition results in actual obliteration of the vessels beyond, and that this, in reality, causes the appearance of lessened irritability.

There are reasons why this view is not tenable. First, if there is complete obliteration of the capillaries in a certain area, complete disappearance of the tissue supplied by these vessels must result, for cellular life is dependent on capillary blood exchange (21). Such is not observed to be the case in the skin of patients with the malignant syndrome of hypertension, however. Second, it has been shown on a large group of patients, with extreme degrees of organic obliterative vascular disease not complicated by hypertension, that the small dermal vessels do not lose, in any way, their ability to respond by reactive hyperemia to local

ischemia (14). Third, a patient has been observed who, despite an advanced stage of hypertension, had unusually sensitive small cutaneous blood vessels (case M. S., Table II).

Another probable supposition is that the agent which causes constriction of arterioles in the malignant phases of hypertension extends its influence to the smaller vessels beyond. A finding which lends some support to this viewpoint is the recent observation of Wilkins and Duncan (9) that angiotonin, injected intracutaneously, causes local blanching, although it is not as marked as that caused by a similar injection of epinephrine. In this regard, we have not only been able to confirm this finding, but to extend it to our studies. By iontophoresis of a small amount of epinephrine into the skin of a normal subject, it is possible to change the responses of the small dermal vessels, as measured in this paper, so as to resemble closely those obtained in the malignant phase of hypertension. That is, the capillary sensitivity decreases greatly and the response to local ischemia is abolished. An attempt was made to duplicate this result with angiotonin, with only partial success. This was due to the difficulty of introducing angiotonin into the skin by iontophoresis.*

Volhard's clinical separation of hypertensive patients into those with red and those with pale skin may have more merit to it than it has been commonly accorded (22). His conception, however, that the color of the skin is mainly dependent upon the caliber of the arterioles is erroneous, as has been properly pointed out by Fishberg (7). On the other hand, his impression that in the later stages of hypertension there appears in the blood stream a vaso-pressor substance which causes universal vaso-constriction finds some support in our studies. Thus, in the early stages of hypertension, the quantitated responses of the small vessels of the skin are no different from those in normal skin, whereas in the malignant phases of the disease they show a marked decrease in sensitivity, indicating an increased tone. Since it is the smaller blood vessels of the skin which determine its color (16), it may be seen that the increases in the tone of these vessels may result in the pale skin of the late phases of hypertension,

observed by Volhard. Just what relationship the degree of renal damage, held to be responsible for these changes by Volhard, has to the responses of the small dermal vessels remains to be ascertained.

These findings of abnormal small cutaneous vessel responses in the extreme stages of hypertension, if confirmed and extended, might supply a reliable criterion of the extent of the vascular lesion in this condition. It might contribute to the answer of the problem of just when an apparently benign hypertension is converted to a malignant phase. The rapidly fatal course of this disease may, in itself, result from eventual involvement of the smallest blood vessels, with all that implies.

SUMMARY AND CONCLUSIONS

The responses to graded mechanical stimulation, and to local ischemia of the smallest blood vessels of the skin of the ventral surface of the forearm, were quantitated in fifty patients with arterial hypertension, twenty-five patients with arterial hypertension associated with arteriosclerosis, and twenty-three patients with arteriosclerosis. Also included in this study were eleven cases of malignant hypertension, and thirteen cases of hypertension associated with various types of nerve lesions, which influenced their capillary sensitivity. These results were compared to similar studies on a suitable control group of thirty-two subjects. The implications of the abnormal responses obtained were discussed. The following conclusions were reached.

1. In the group with arterial hypertension, it was demonstrated that the responses of the small dermal vessels, as quantitated in this study, are in no way significantly different from those of a comparable normal group.

2. No relationship was found between the severity of the hypertensive process, excluding the malignant phase, and the functional responses of the small cutaneous vessels. Many cases of very severe hypertension, with diastolic blood pressures of over 130 mm. of Hg, were studied, and showed normal capillary responses.

3. The conclusions for the purely hypertensive group apply as well to those patients with hyper-

* Unpublished observations. Angiotonin was generously supplied to us by Dr. Irvine H. Page of the Lilly Medical Research Laboratories.

tension associated with arteriosclerosis, and with uncomplicated arteriosclerosis.

4. Of eleven patients with the malignant syndrome of hypertension, ten had small blood vessel responses which indicated greatly decreased sensitivity. This was especially evidenced, in five of these patients, by a complete inability of the small dermal vessels to respond by reactive hyperemia to local ischemia.

5. Thirteen patients with hypertension complicated by a nerve lesion, ranging from a cerebral vascular accident to Parkinson's disease, were found to have small cutaneous vessels as much as eighteen times more sensitive than the normal or hypertensive groups. Very irritable, small, dermal blood vessels may therefore exist even in the presence of arterial hypertension.

6. The above conclusions suggest that the humoral agent now believed responsible for arterial hypertension does not exert its influence upon the smallest blood vessels in the benign stages of the disease but may do so in the later malignant phase. If this is confirmed, the quantitative responses of the small dermal blood vessels might serve as a criterion of the extent of the vascular lesions in advancing hypertensive disease.

BIBLIOGRAPHY

1. Ellis, L. B., and Weiss, S., The measurement of capillary pressure under natural conditions and after arteriolar dilatation: In normal subjects and in patients with arterial hypertension and with arteriosclerosis. *J. Clin. Invest.*, 1929, 8, 47; and also, *Am. Heart J.*, 1930, 5, 448.
2. Wiggers, C. J., The dynamics of hypertension. *Am. Heart J.*, 1938, 16, 515.
3. Griffith, J. Q., Jr., Roberts, E., and Corbit, H. O., Studies of criteria for classification of arterial hypertension. I. Cutaneous capillaries. *Am. Heart J.*, 1941, 21, 47. II. Minute vessel pressure. *Ibid.*, 1941, 21, 54.
4. Eichna, L. W., and Bordley, J., III, Capillary blood pressure in man. Direct determination in the digits of subjects with normal and elevated arterial pressures. *J. Clin. Invest.*, 1941, 20, 458.
5. Boas, K., and Mufson, I., The capillary blood pressure in arterial hypertension and in nephritis. *J. Lab. and Clin. Med.*, 1923, 9, 152.
6. Mufson, I., A study of the capillary pressure in nephritis and hypertension. *Am. J. M. Sc.*, 1932, 183, 632.
7. Fishberg, A. M., Hypertension and Nephritis. Lea and Febiger, Philadelphia, 1931, 2nd Ed.
8. Cowdry, E. V., Editor, Problems of Ageing. Biological and Medical Aspects. Williams and Wilkins, Baltimore, 1939.
9. Wilkins, R. W., and Duncan, C. N., The nature of the arterial hypertension produced in normal subjects by the administration of angiotonin. *J. Clin. Invest.*, 1941, 20, 721.
10. Griffith, J. Q., Jr., The frequent occurrence of abnormal cutaneous capillaries in constitutional neurosthenic states. *Am. J. M. Sc.*, 1932, 183, 180.
11. DiPalma, J. R., Reynolds, S. R. M., and Foster, F. I., Sensitivity of the smallest blood vessels of the human skin: Responses to graded mechanical stimulation in normal males. *J. Clin. Invest.*, 1941, 20, 333.
12. DiPalma, J. R., Reynolds, S. R. M., and Foster, F. I., Quantitative measurement of reactive hyperemia in human skin: Individual and seasonal variations. *Am. Heart J.*, 1942, 23, 377.
13. DiPalma, J. R., and Foster, F. I., The segmental and ageing variations of reactive hyperemia in human skin. *Am. Heart J.*, 1942, 24, 332.
14. DiPalma, J. R., and Foster, F. I., A reactive hyperemia ring test in the study, evaluation and prognosis of pedal lesions caused by obliterative vascular disorders. *Am. Heart J.*, 1942, 24, 345.
15. Riseman, J. E. F., and Weiss, S., The age and sex incidence of arterial hypertension. *Am. Heart J.*, 1930, 5, 172.
16. Lewis, T., The Blood Vessels of the Human Skin and Their Responses. Shaw, London, 1927.
17. Adson, A. W., and Allen, E. V., Essential hypertension. General considerations. *Proc. Staff Meet., Mayo Clin.*, 1937, 12, 1.
18. Derow, H. A., and Altschule, M. D., The nature of malignant hypertension. *Ann. Int. Med.*, 1941, 14, 1768.
19. Mainland, D., The Treatment of Clinical and Laboratory Data. Oliver and Boyd, Edinburgh, 1938.
20. Fisher, R. A., and Yates, F., Statistical Tables for Biological, Agricultural and Medical Research. Oliver and Boyd, Edinburgh, 1938.
21. Weiss, S., and Frazier, W. R., The density of the surface capillary bed in the forearm in health, arterial hypertension and in arteriosclerosis. *Am. Heart J.*, 1930, 5, 511.
22. von Volhard, F., Der arterielle Hochdruck. Verhandlungen der Deutschen Gesellschaft für Innere Medizin. Verlag von J. F. Bergmann, München, 1923.