The Determination and Evaluation of Capillary Resistance—A Review of Methodology

By Jenő Kramár

Since the diagnostic significance of “fragile capillaries” was first recognized,¹,² much productive work has been accomplished to improve the methods for determination of capillary resistance and to elucidate the variables concerned. Strangely enough, these studies have led to little practical application. The current clinical routine for measuring capillary resistance continues with the same shortcomings as of old: (1) There is still no firm agreement as to the most suitable method; (2) the procedure is not standardized, hence findings of various investigators are difficult to compare; (3) pitfalls incidental to the testing are not generally appreciated; (4) interpretation of findings is not uniform and frequently erroneous. This is all the more deplorable because these tests still constitute useful tools for experimental studies of hemorrhagic disorders as well as for the clinical approach to the question of whether a vascular abnormality may be present. In addition, recent observations suggesting that increased capillary resistance may also represent abnormal conditions broaden the field of application of capillary resistance measurement beyond that of clinical and experimental hemorrhagic disorders.

The purpose of the present paper, which is the result of ten years’ clinical and experimental studies, is to draw practical conclusions and to suggest how the present unsatisfactory situation can be improved. References are limited to data directly pertinent to the topics discussed and, since excellent review articles are available,²⁰,²⁴,²⁹ no attempt is made to review the extensive literature.

(1) Methodology

As to the question of the most suitable method for measuring capillary resistance, the discussion will be limited to the two methods most generally used, the pressure (tourniquet)²⁶,¹⁸ and the suction³ methods.* Several attempts have been made to compare and correlate these methods with vague or contradictory results.²,⁷,²³,²⁸ Consequently a study was made on 132 healthy normotensive adults of both sexes by both the pressure and suction methods simultaneously as specified in figure 1. It was found that although there is no rectilinear correlation between the two methods in a sense which would always permit direct or individual plotting of the number of petechiae against the

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*The often used but illogical term “negative pressure method” is deliberately avoided as well as the redundant adjective in the term “positive pressure method.”
Fig. 1.—Comparison of the pressure and suction technics for determination of capillary resistance on 132 healthy normotensive adults of both sexes. Each plotted cross represents the dual simultaneous results obtained by both technics. In the pressure method the number of petechiae, in the suction method the least degree of suction (in cm. Hg) sufficient to elicit one or more petechiae, served as indicator. Capillary resistance was defined as low whenever, under standard conditions as outlined below, at least five petechiae appeared by the pressure technic, or when the capillary resistance value was less than 8 cm. Hg by the suction technic.

degree (cm. Hg) of suction, there is a very good curvilinear correlation. As shown in figure 1, positive results were obtained by the pressure method in all subjects whose capillary resistance values were less than 8 cm. Hg by the suction method. Contrariwise, the pressure method never yielded positive findings in any subject with capillary resistance values greater than 21 cm. Hg by the suction method. A gradual transition was noted in the intermediate zone (8–21 cm. Hg), i.e., in the large group of average individuals. Using
\[ r_{xy} = \frac{\sigma_{xy}}{\sigma_x \sigma_y} \]
to compute the coefficient of correlation and
\[ \sigma_y = \frac{1 - r^2}{\sqrt{N - 1}} \]
for the standard error of correlation, an index correlation of 0.808 was obtained.
with a standard error of 0.030. The relationship can be interpreted very much like the Pearson product-moment, indicating that a substantial relationship exists which, as demonstrated by the low standard error, cannot be due to chance alone. The low standard error also confirms that the obtained correlation is close to the total population coefficient.

A study of the possible mechanism involved in the suction method has thrown some light on this correlation. Using a binocular operation microscope with built-in illumination, the minute vessels, including the capillaries of the ear lobe or the mesoappendix of the rat, were visualized. A miniature transparent plastic suction cup (inner diameter, 2 mm.), connected to a suction device and a manometer, was then placed on the surface of the visualized field so that the vessels were clearly visible through the suction cup before, during and after suction. The following changes were noted. The skin or mesoappendix area within the cup was slightly raised at the moment the suction began, the capillary network became engorged, eventually to the point of rupture. Scrutiny of the area exposed to the suction and its vicinity immediately after suction was discontinued and the cup removed clearly revealed a ring-shaped zone caused by the pressure of the brim of the cup around the circular area upon which the suction was applied. In this ring-zone the venules still appeared compressed and bloodless for a brief time whereas the arterioles showed an unimpeded flow. Evidently, by virtue of the suction the area of the skin or mesoappendix within the suction cup was lifted and this resulted in a distortion of the ring-zone corresponding to the brim of the cup. This distortion, in turn, depending upon the degree of suction, hampered or even interrupted venous flow but did not significantly interfere with arterial flow. That the ultimate cause of rupture of the vessels and hemorrhage was not the suction per se, but rather the increased intracapillary pressure, was confirmed by the finding that if too high a suction was applied, no hemorrhage occurred inasmuch as the arterioles were also compressed and the capillary pressure could not rise. It seems, therefore, that the pressure and suction methods both rest upon the same underlying phenomenon, the difference being only that capillary pressure is increased in the pressure method by a tourniquet involving the entire arm, whereas in the suction method it is increased by the brim of the suction cup and only in the area limited by the cup. In this sense the suction method is in reality a miniature pressure method.

Despite the common underlying phenomenon and good correlation, the two methods differ widely in their relative merits of practical application. The advantages of the pressure method are that it does not require a special device, and that it puts all the skin capillaries of the arm to the test. But its disadvantages are overwhelming. It is cumbersome, may cause considerable discomfort, and is often resented by children. Its results are rather vague and oftentimes cannot be duplicated. After both arms have been used, a long waiting period must precede the next measurement. Finally it cannot be applied in experimental animals. In our experience, the pressure method can serve only for crude estimations of capillary resistance. A detailed study requiring more accurate values or necessitating repeated testings, often at short intervals, clearly demands the suction method as the method of choice.
The influence of polyunsaturated fatty acids, the effects of stress and endocrines upon the capillaries, the stress-induced changes in capillary sensitivity to corticosteroids, the relation of capillary resistance to the activity of the platelets—none of these could have been reliably recognized by the pressure method on the human, nor studied at all on experimental animals. In addition, the state of abnormally high capillary resistance which, as described below, is also significant, can be recognized only by the suction method.

(2) Standardization

Scarcely another routine diagnostic method is so replete with technical uncertainty as that which is supposed to measure capillary resistance. Numerous variations of both the pressure and suction methods exist and many of them in turn have been further modified. Despite its obvious desirability, standardization has not yet been attempted. Perhaps a recommendation by an appropriate scientific body is necessary as an initial step.

One might predict that agreement on the most suitable pressure method will not be difficult since the procedures suggested by most textbooks and routinely used by most clinicians represent but minor variations of the Göthlin test as modified by Wright and Lilienfeld. Tourniquet on upper arm inflated midway between systolic and diastolic pressures for 15 minutes, petechiae counted 5 minutes later in an outlined circular area of 2.5 cm. diameter with upper margin 4 cm. below the elbow crease. Closer scrutiny, however, proves the task to be rather difficult. There might be no disagreement as to the desirability of a minimum compression time. A 15-minute compression, as routinely applied, is in our experience too long and needlessly uncomfortable. We found that by increasing the skin area to 3 cm. diameter, the compression time could be reduced to 5 minutes without impairing results—a great advantage for both observer and patient. Standardization of the degree of compression which would be universally applicable seems to be, however, a greater task. A pressure corresponding to the mid-pulse pressure, as practiced routinely, is obviously valid only in normotensive subjects. Hypertensive patients' capillaries may be subjected to undue strain in this manner. To avoid this, general use of a standard pressure which is independent of the blood pressure would appear preferable, e.g., 90 mm. Hg as suggested by Miyake and Kojima. However, this may be too high in hypotensive individuals and certainly so in the lower half of the pediatric age range. An acceptable standard pressure must, therefore, obviously lie below 60 mm. Hg, e.g., as applied in the two-stage technic of the modified Göthlin method (Griffith and Lindauer). In order to obtain a significant number of petechiae at this low pressure, however, a longer compression time and a larger observation area are required. The first, though uncomfortable, would be acceptable; the second, on the arm of an infant or small child, would be prohibitive and necessitate another standard

*In our comparative study of the pressure and suction methods as described above, this pressure was used since all subjects were healthy and normotensive.
for this age with a much reduced observation area and considerably lengthened compression time.

It may be less difficult to decide on the best suction method. The following should be considered: (a) the most appropriate body site as the standard observation area; (b) a suction cup small enough to allow several consecutive measurements and at the same time large enough to facilitate free visualization of petechiae; (c) the shortest effective suction time; and (d) compact, simple and inexpensive equipment.

In the following, details of the method and procedures are described which, we believe, approximate these requirements. This has been the routine way of measuring capillary resistance both clinically and in experimental animals in our laboratory during the past 10 years. It has yielded reliable and easily reproducible results in the hands of all investigators in our group.

(a) \textit{Standard site of testing.} A triangular area is delineated on the proximal volar aspect of the forearm. The base of this triangle runs parallel and approximately 2 cm. distal to the cubital flexion crease, the sides being the creases of the extensor and flexor groups of muscles of the wrist and the hand. The apex of the triangle is then approximately in the middle of the forearm. In infants and small children the site of choice is the subclavicular area. Values obtained in this area are, in our experience, essentially the same as those observed on the forearm.

(b) \textit{The suction cup.} Transparent plastic suction cups, improvised from rods or tubes, with an inner diameter of 7 mm. and outer diameter of 13 mm. were found most suitable. Such a cup is so compact that about 25 readings may be obtained on one arm, enough for about five individual measurements.

(c) \textit{The duration of suction} was also studied. One minute was found to be both efficient and time saving. A shorter suction is not fully effective whereas longer suction is unnecessary and uncomfortable.

(d) \textit{The apparatus} should consist essentially of a 100-ml. vacuum reservoir connected to a suction pump, a suction cup, and an intercalated mercury manometer. The reservoir was found to be essential. It compensates for the slight leakage which despite use of lubricant unavoidably occurs at the site of contact between the brim cf the suction cup and the skin, and thus maintains a constant level of suction. Our portable clinical devices were improvised by the use of a vacuum bottle, a hand suction pump and a manometer registering suction up to 60 cm. Hg. Standard devices similar to a blood pressure apparatus of either the mercury manometer or the aneroid type, with a built-in double-walled bottom compartment cf the box serving as reservoir, could be readily manufactured. For experimental animal studies we have used a motor-powered device which permits simultaneous measurements on three animals by different observers.

The least suction (in cm. Hg) applied for one minute and producing one or more petechiae under the described standard conditions was considered the value of capillary resistance. In most instances this could be determined by four to five readings. When the subject's previous capillary resistance value was unknown, the suction was set first to an average level (15 cm. Hg)
and the least effective suction determined in a stepwise manner. The procedure is illustrated by the following four examples.

(1)

15 cm. -  
20 cm. -  
25 cm. +  
23 cm.  
22 cm. -  

(2)

15 cm. +  
10 cm. -  
12 cm. -  
13 cm.  
8 cm. +  

(3)

15 cm. +  
10 cm. +  
5 cm. -  
7 cm. -  

(4)

15 cm. -  
20 cm. +  
18 cm. -  
19 cm. -  
20 cm. 

*Cap. res. value*  
23 cm.  
13 cm.  
8 cm.  
20 cm.

It was made a rule to avoid re-use of the same skin area within a 24-hour period. In serial readings, therefore, the area tested was marked and the adjacent one used for the next testing.

As to reliability, measurements repeated on the same arm at short intervals were found to deviate by ± 1 cm. at most. This may be considered the error of the method. When both arms were tested comparatively, an average difference of 1.6 cm. was found, the maximum deviation being 3.5 cm. There was no correlation between the higher figure and the predominate arm. In daily follow-ups, the higher figures were not even found consistently on the same arm.

(3) *Pitfalls of Capillary Resistance Determination*

A common pitfall is unawareness of the fact that increased capillary resistance may be simulated or low capillary resistance camouflaged by a transitory spasm of the precapillary arterioles. As discussed under (1), in this case the intracapillary pressure in the skin area within the suction cup cannot be raised by the suction, hence bleeding may fail to occur with a degree of suction which otherwise would be more than sufficient to cause capillary rupture. This is a frequent and characteristic finding in tense, nervous individuals and may lead to difficulties similar to those encountered when blood pressure is measured in such persons. In this situation one may easily assume a negative result and further increase the suction. Petechiae will then first appear at the moment when the spasm has resolved and the degree of suction at which this occurs may be erroneously considered the value of capillary resistance. The phenomenon is easily recognized. Ordinarily the skin within the suction cup flushes when suction is applied and remains flushed for a while even after removal of the cup. In arteriolar spasms the skin remains pale. This phenomenon is also suggested by the finding of a strongly positive capillary test occurring with a degree of suction at or above which previous readings were negative. Minor degrees of this condition were commonly found at first reading. Many of the individuals concerned responded normally at subsequent testings; some, however, maintained their characteristic pattern and caused us to interrupt testing until relaxation occurred.

False negative readings and, consequently, erroneously high capillary resistance values are also obtained when initial suction is too high, sufficient to
compress not only the venules but also the arterioles. The result is the same as with arteriolar spasm.

4) Interpretation of the Measurement of Capillary Resistance Values

The result of an individual measurement may fall into one of three categories: capillary resistance may be high, medium or low. The criteria of categories vary according to the method employed and the standards observed. Using the pressure method as described under (2), more than five petechiae are routinely considered as a sign of "abnormal" fragility (or low resistance) of the capillaries. Although further distinction may be attempted within the fragile and nonfragile groups on the basis of the number of petechiae, a reliable graduation is hardly feasible. Using the suction method as standardized in our laboratory and described under (2), medium capillary resistance values are considered to range between 8–21 cm. Hg. Values below 8 cm. and above 21 cm. are regarded as being low or high, respectively.

To properly evaluate the measurements, one must be aware of the following facts. Capillary resistance is subject to physiologic variations.13 It tends to decrease as the day advances, apparently as the result of the diurnal rhythm of adrenocortical activity. It may fluctuate from day to day due to variations in the strain factor of everyday life. It shows seasonal variations with a tendency in the temperate zone to decrease in the late winter and early spring.

Capillary resistance undergoes changes by virtue of stressful stimuli, physical as well as emotional, for a period of a few hours (immediate capillary stress response) or for several days (late capillary stress response13). Although these responses may be of manifold patterns, an increase in capillary resistance—oftentimes considerable—is the most common response in the human as well as in several animal species. In the immediate response, the underlying cause seems to be a sudden vasopressin discharge with an interplay between vasopressin and histamine. The late response appears to be due to an increase in the corticosteroid production and/or in the sensitivity of the capillaries (as target organ) to the available corticosteroids.16

Capillary resistance is influenced by endocrines.15,24 In general, anti-inflammatory corticosteroids (the 17-OH-corticosteroids) are also capillary-active in that they increase capillary resistance to unusually high levels.14 In contrast, the somatotropin hormone decreases capillary resistance and is capable of antagonizing the capillary effect of the corticosteroids.15

Capillary resistance has individual characteristics in the human.13 There are healthy persons with high and others with medium or low capillary resistance and each tends to maintain his or her individual level. If capillary resistance deviates from this level, owing to one or more of the factors discussed above, it is likely to return to the original level sooner or later. It is an important fact that at least 8 per cent of healthy individuals with no bleeding tendency whatsoever, nor a history of it, have low capillary resistance levels which one expects to find, as a rule, only in the presence of a hemorrhagic tendency. On the other hand, it must also be realized that very high values of capillary re-
Resistance may have diagnostic significance—a possibility that has not emerged previously. They may indicate excessive stress, or increased corticosteroid activity on a pathologic basis. Interpretation of capillary resistance measurement for the differential diagnosis of hemorrhagic disorders requires particular caution. First of all it must be realized that these tests are unsuitable for the detection of (a) localized anatomic abnormalities of the capillaries as in hereditary telangiectasia, (b) circumscribed toxic inflammation of the capillary wall as in anaphylactoid purpura, (c) embolic processes in the capillaries as in septic, viral or rickettsial diseases, and (d) inability of the capillaries to contract upon injury as in vascular pseudohemophilia. Presence or absence of these conditions must be demonstrated by the over-all clinical and hematologic picture and by capillary microscopy.

In the absence of the above conditions, however, a capillary resistance lying in the physiologic high range (21-45 cm.) has a great diagnostic significance: it rules out vascular participation in a bleeding tendency. This is also true for the newborn period, but the unusually high physiologic capillary resistance level at this age must be considered.

The finding of low capillary resistance (less than 8 cm.) in case of a bleeding tendency suggests only that a vascular factor may or may not be present. However, a capillary factor may be postulated with high probability even in this case if the patient's previous normal individual level is known and a definite decrease has been observed with the onset of the disease, or if parallel with the patient's improvement the low capillary resistance is found to increase gradually up to a steady high level which later proves to be the patient's normal (individual) level.

It is obvious that failure to consider the foregoing facts may easily lead to misinterpretation of capillary resistance measurements. To avoid such errors, the following basic points should be kept in mind.

In routine examination of a patient, presence of the factors known to influence capillary resistance (stress, endocrine imbalance or hormonal treatment) must be ruled out or recognized and, if possible, eliminated. In repeated measurements, the physiologic variations should be considered. Unusually high capillary resistance (50 cm.), barring precapillary spasm or error in technic, should also be appreciated. In the routine diagnosis of hemorrhagic disorders, the above criteria are justified and practicable. In experimental work in which capillary resistance of humans or experimental animals is studied with relation to nutrition, hormones, drugs or any other influencing factor, the individual capillary resistance level and the degree of physiologic fluctuations must first be established by daily testings for about one week. These values will then serve as a baseline. Only deviations lying significantly above or below the baseline and beyond the established fluctuations can be possibly correlated with the factor studied.

In retrospect one may gather the impression that the significance of capillary resistance determination as a clinical tool has become more limited as our knowledge of this method has increased. This may be true especially with
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regard to the diagnosis of hemorrhagic disorders. However, it must also be realized that proper application of this tool and more careful evaluation of the findings have rendered the latter more accurate and reliable. In addition, as demonstrated in our studies and confirmed by the investigations of Wilhelm's group, capillary resistance measurement has acquired a broader field of application in experimental medicine; it helps not only to determine the nature of a bleeding tendency but serves also as a useful tool in experimental studies involving the capillaries as the target organ.

Summary

In view of the uncertainty and inadequacy still prevailing in the routine determination and interpretation of capillary resistance, the problem has been analyzed in the hope of contributing to a much needed improvement.

(1) The pressure and suction methods have been compared and a good correlation found. A study of the mechanisms involved reveals that both methods rest upon a common underlying mechanism. The suction method is in reality a miniature pressure method.

(2) Scrutiny of the merits and shortcomings of the two methods leads to the conclusion that the pressure method can serve only for crude estimations of capillary resistance. Detailed clinical studies of capillary resistance requiring repeated accurate measurements at short intervals, as well as experimental animal studies, necessitate the suction method as the obvious method of choice.

(3) The three main causes of the present undesirable situation in this field are discussed: lack of standardization; inadequate realization of the pitfalls of testing; and erroneous interpretation of findings.

Summario in Interlingua

Viste le incertitude e le inadequatia que es ancora prevalente in le routinari determination e interpretation de resistentia capillar, un analyse del problema esesva interprendite in le spero de contribuer a un melioration que es multo necessari.

1. Le methodos a pression e a suction esseva comparate e un bon correlation inter illos esseva trovate. Un studio del mechanismos de iste methodos revele que le duo depende del mesme mechanismo subjacente. Le methodo a suction es in effecto un methodo a pression in miniatura.

2. Un scrutinio del meritos e del disadvantages del duo methodos duce al conclusion que le methodo a pression pote fornir solmente crude estimationes del resistentia capillar. In detaliate studios clinic de resistentia capillar que require precise mesurationes repetite a curte intervallos, si ben como in studios experimental in animales, le methodo a suction es le obvie methodo de election.

3. Es discutite le tres causas principal del presente indesirabile situation in iste campo: manco de standardisation; inadequate appreciation del causas de error in le tests; e erronee interpretation del resultatos.
REFERENCES

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Jenő Kramár, M.D., Professor of Pediatrics, The Creighton University School of Medicine, Omaha, Neb.
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JENŐ KRAMÁR