AN ANALYSIS OF CRITICAL CLOSURE IN THE ISOLATED DUCTUS ARTERIOSUS

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INTRODUCTION

The term critical closure was coined by Burton (1961) to describe the supposed instability arising in a blood vessel when active tension was present. The model proposed by Burton has now been used by him and his coworkers (Burton, 1951, 1954; Nichol, et al., 1951) to explain the phenomenon of cessation of flow through a vascular bed subjected to a positive driving pressure. The model applies specifically to a single vessel rather than a vascular bed so that a direct test has not been possible. The present work consists of an analysis of the forces in a single isolated vessel which is capable of occluding its lumen due to the action of its muscular wall. Although the model developed here differs substantially from that of Burton, the name critical closure is retained because the behavior described herein is adequate to account for all the experimental findings reported under that name.

The work is in three parts. The first is the theoretical development of the vessel wall tension-radius relationship in terms of the distribution in the vessel wall of muscle fibers whose individual length-tension relationships are similar to those of other muscle preparations. The second part is the discussion of the equivalent of Burton's "Laplace's law" for a thick-walled vessel. This part is actually an adaptation of Fung's (1968) derivation for thick walled cylinders to the case of ropy structures. The third part is the application of these theoretical equations to actual data from a vascular smooth muscle preparation, and the prediction of radius-pressure plots from the measured tension-radius relationship.

THEORY

The following definitions are employed throughout the text:

V_e volume of an element in the wall of a vessel
r radius at which the element resides
δ thickness of an element in the wall

l	tube length of the vessel segment
A_e	cross sectional area of an element in the wall
a	internal radius of vessel (variable)
b	external radius of vessel (variable)
A	cross sectional area of vessel wall
σ_t	tangential stress in vessel wall
σ_r	radial stress in vessel wall
P_i	internal pressure with respect to atmosphere
P_o	external pressure with respect to atmosphere
$F(r)$	the total force which would be developed by an equivalent muscle of length $2\pi r$
T(a)	the total tension present in the wall of a vessel as a function of the internal radius

Tension Development of a Circular Muscle

Fig. 1 *a* is a diagram of a lineal muscle. The properties of such a muscle which are pertinent to this discussion are as follows: (*a*) the volume is constant and (*b*) the tension depends on the length. The force developed in extension is some determinate function of length. Secondly, the force in compression is zero. Thirdly, the rest length is not zero. The muscle force also depends on various time dependent factors as well, but the discussion will be restricted to steady-state relationships. The dependency of tension on length is called the static length tension relationship. It may, in principle, be determined on either a stimulated or an unstimulated muscle and the above statements are true in either case.

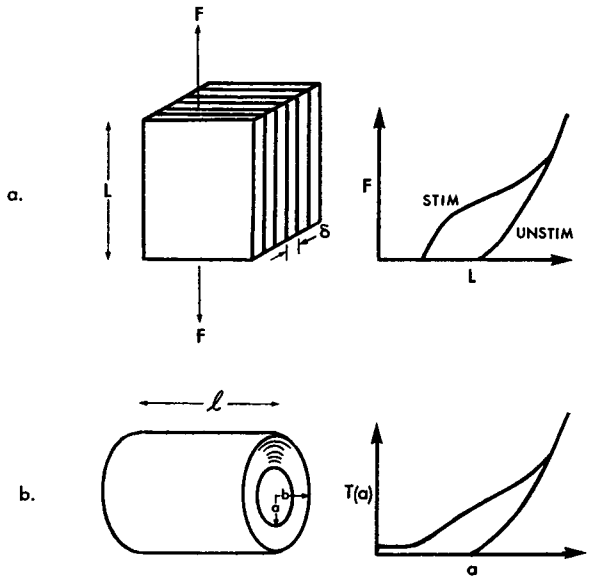

FIGURE 1 *a* Diagram of a "typical" lineal muscle, and its force-length diagram. 1 *b* An equivalent circular muscle derived from the lineal muscle by uniting the ends; with a plot of total tangential wall tension versus the internal radius *a*.

The muscle is supposed to be divisible into identical infinitesimal laminae. The total tension is the sum of the tensions in these laminae which may be expressed as an integral. In the linear muscle the tension in all the laminae are identical and the integral is taken over uniform intervals. Now suppose the two ends of the muscle to be brought together to form a cylindrical muscle with the laminae forming concentric cylinders (see Fig. 1 *b*). In this case, the total tension is still the sum of the elemental tensions, but the elemental tensions are no longer identical because the elements are of different length. In addition the intervals (of radius) are no longer uniform. The elemental volume is

$$V_e = 2\pi r \delta l. \tag{1}$$

In general both δ and l will be dependent on r if V_e is constant. The dependency of δ on r cannot be directly measured but it must complement the dependency of l on r. Since in the experiments described later l was constant it will be taken to be constant and unity in the remainder of the theoretical discussion. Therefore

$$\frac{V_e}{l} = A_e = 2\pi r \delta \tag{2}$$

It is seen that δ is a function of r. Therefore, if the elemental force is expressed as a function of r it is necessary to introduce a distribution function to allow for the dependency of the interval on r. If, in addition, the integrated tension is divided by the total number of elements the total force relationship may be used rather than the elemental relationship. This last modification is merely a matter of scaling. The assumption that all of the elements have equal volume and equal rest length is arbitrary and made to simplify the analysis. A more accurate model would be that each element is at its individual rest length in the fully relaxed vessel. It would remain true, however, that the elements near the outer surface would decrease in length only slightly as compared to the inner elements and the constant volume assumption would give rise to similar changes in distribution to those proposed. The more accurate model would greatly complicate the analysis by requiring that all changes in length or thickness be expressed as changes from the rest state. In fact, this would make very little difference in the result since the difference between the inner and outer radii is relatively slight in the relaxed vessel and the initial state is very nearly the same for all elements.

The other somewhat controversial assumption is that the force of the muscle and not the stress is a function of length. If the stress or force per unit area were a function of length then it would not be necessary to take into account the elemental distribution since the elemental area would increase by the same amount as the density of elements decreased. In skeletal muscle however it is well established that the number of interacting elements does not change with length and therefore changes in cross section with shortening or lengthening do not affect tension de-

velopment. Although this behavior has not been established for smooth muscle it is implicit in this analysis.
If

$$\delta = \frac{A_e}{2\pi r} \tag{3}$$

then the density of elements is the reciprocal of δ

$$g(r) = \frac{2\pi r}{A_e} \tag{4}$$

The total number of elements is the integral of $g(r)$ so that the total tension in the wall may be written

$$\frac{\frac{2\pi}{A_e}\int_a^b rF(r)\,dr}{\frac{2\pi}{A_e}\int_a^b r\,dr} = T(a). \tag{5}$$

Since the lower integral is a constant, the limits are not independent and the total tension can be expressed in terms of either the internal or external radius.

The above equation expresses the relationship between the total tension in a cylindrical muscle and in an equivalent lineal muscle. If one is presented with a cylindrical muscle and wishes to know the length-tension relationship of the equivalent lineal muscle it is possible to differentiate the above equation

$$\frac{dT}{da} = \frac{2\pi}{A}\left[bF(b)\frac{db}{da} - aF(a)\right] \tag{6}$$

$$\frac{db}{da} = \frac{a}{b}$$

$$\frac{dT}{da} = \frac{2\pi a}{A}[F(b) - F(a)]. \tag{7}$$

From the description of a typical muscle we know that $F(a)$ becomes zero at the radius corresponding to the rest length of the lineal muscle. This radius will be called the critical radius c. When $a \leqq c$

$$\frac{dT}{da} = \frac{2\pi a}{A}F(b) \tag{8}$$

In this form all terms may be measured except $F(b)$ which can thus be found. The

analysis is limited because the relationship can only be used when a is on the interval

$$0 \leqq a \leqq c.$$

Unless the preparation has an exceptionally thick wall this range of values for $F(b)$ will allow an extrapolation to be made to the zero force intercept which in turn defines c. The earlier definitions of a typical muscle imply some interesting properties for the region of the wall within the radius c. Since the muscle is assumed to develop no force in compression this region is essentially liquid with respect to radially acting forces. However, since the wall is fixed in position the region still contributes to resistance to flow through the lumen. The importance of this property will become apparent in the development of the pressure-tension-radius relationship which follows. It should be pointed out that while the foregoing derivation of the properties of a circular muscle allow one to obtain a value of the rest radius, this is not the only way in which c can be determined. The slack radius could also be determined histologically by inspection of cross sections for slack appearing fibers. However such histological techniques would introduce additional problems, such as dehydration and fixation artifacts which would need to be allowed for.

Pressure-Tension-Radius Relationsip (Isobar Equation)

The relationship between the internal and external pressures and radial and tangential stresses in a thick-walled vessel was obtained by Lame and Clapeyron in 1847 for the case where Poisson's ratio and Young's modulus for the material are constant and the deformations small. Such assumptions are obviously in error for a material such as the wall of the ductus. In recent work (Crisp, 1968; Fung, 1968) techniques have been developed for determining these relationships in structures similar to the ductus, given that the stress-strain history relationship of the material is known. Some speculations could be made on the basis of the tension-radius diagram about the stress-strain relationships of the ductus material. Perhaps by imposing an arbitrary past history, the material could be made to behave like a simple nonlinear viscoelastic substance. However, for the purpose of analyzing critical closure phenomena this is not necessary. As was pointed out by Fung (1968), the ntegral of the stress distribution is independent of nonlinearity or past history, as long as equilibrium states only are considered. The integral of the stress through the wall, i.e., the total wall tension may be expressed

$$T(a) = P_i a - p_o b. \tag{9}$$

However, if the internal radius a is less than the slack radius c, the region of the wall between c and a does not contribute to the total tension and we may write

$$T(a) = p_i c - p_o b \qquad a \leqq c. \tag{10}$$

Since the region of the wall between a and c is slack, it will support negligible radial shear and the pressure is transmitted unimpeded to the radius c. However, the slack region is attached to the vessel wall and still contributes to the fluid impedance of the vessel.

If the external pressure is negligible, the above pair of equations become the following

$$T(a) = \begin{matrix} p_i a & a \geqq c \\ p_i c & a < c. \end{matrix} \qquad (11)$$

It is possible to measure the function $T(a)$ in an actual vessel and determine c by solving equation 8 for the same vessel, thus predicting the entire relationship between pressure and radius and determining especially if the vessel is capable of closing against a positive transmural pressure. If c can be measured by some other means and the pressure-radius relationship determined experimentally, then $T(a)$ can be calculated. Since the above relationship defines lines of constant pressure on a tension-radius plot, the term isobar function will be used to refer to it.

METHOD

The preparation chosen for this study was the ductus arteriosus of the foetal guinea pig. The histology of this preparation has been thoroughly investigated (Holmes, 1958; Kennedy and Clark, 1941) in relation to earlier studies on its mechanism of closure. It differs from the major vessels primarily in that it has a much larger proportion of smooth muscle to elastin. The preparation was also examined using a modified Masson's trichrome stain. In these preparations the smooth muscle stain was roughly 10 times as extensive as the strains for elastin and collagen. The composition seems to be more similar to that of the small resistance vessels or precapillary sphincters than to the other large vessels. This of course is all to its advantage in this modeling study.

Animals were full term fetuses of mongrel guinea pigs. The fetuses averaged 90 g in weight. Occasional animals were as large as 140 g; animals below 50 g were rejected as immature. The mothers were killed with a blow to the base of the skull and the fetuses were delivered immediately by cesarean section. If the fetuses survived birth, they were placed in a cage for a few hours until needed. No irreversible changes in the ductus were observed for at least 24 hr following birth. Fetuses were killed with a blow to the head, and the chest opened. Considerable care was taken during the dissection not to place undue strain on the ductus itself. The thymus was cleared away and the pericardium removed. With the aid of a low power binocular microscope the descending aorta was severed on either side of the attachment of the ductus and a small portion of the pulmonary artery was removed together with the ductus and aorta segment to a dissection dish, where a ring was cut from the ductus midway between its attachments and mounted around one of the transducer connection wires. This assembly was then transferred to the muscle chamber where the transducer connections were completed. The ductus segments weighed approximately 1 mg and had a diameter (OD) in the animal of 2–4 mm. The diameter is difficult to estimate because the ductus contracts during dissection.

Perfusate flowed continuously through the muscle chamber and the used perfusate was discarded. The perfusates could be quickly switched from O_2 equilibrated to N_2 equilibrated physiological salt solutions. These solutions served as the stimuli to the preparation (McIntyre,

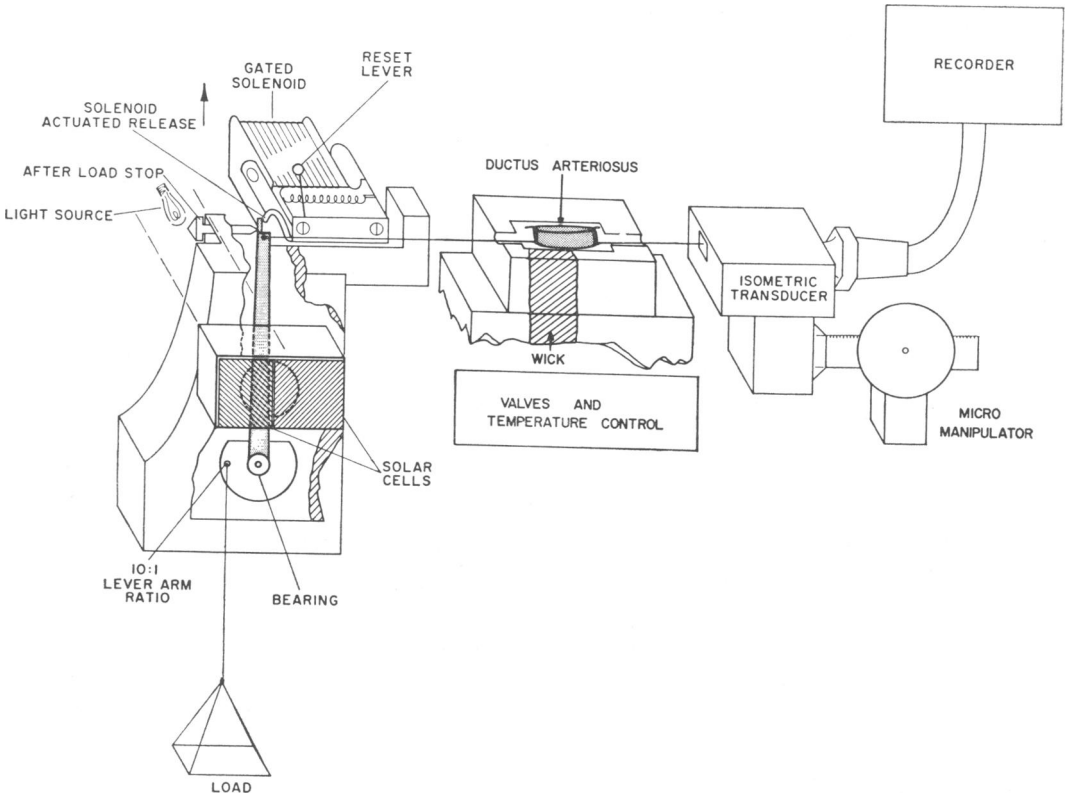

FIGURE 2 Diagram of connections between the preparation and the tension and length transducers. Additional description may be found in the text.

1965; Kovalcik, 1963). The salt composition of the perfusate was (mM) NaCl-130, KCl-5, $MgSO_4$-1, $NaHCO_3$-5, $CaCl_2$-2, and NaH_2 PO_4-0.5. The gases bubbling the perfusates both contained 2% CO_2 and the primary buffer was the CO_2-bicarbonate system buffering at pH 7.2. The muscle chamber was maintained at constant temperature of 35°C.

As shown in Fig. 2, the muscle was mounted horizontally between two transducers. The isotonic lever was of the low inertia type with a 10:1 lever ratio and a bell-crank arrangement to allow horizontal operation. Photodetection using two solar cells differentially was employed for the length signal. The lever was equipped with a magnetically actuated catch which could be withdrawn at any time by actuating the solenoid. If the catch was in place, the system was isometric. The isometric transducer was a variable air capacitance type with a circuit detector (Photocon Dynagage DG600, Photocon Research Products, Pasadena, Calif.), which has been described by M. Schilling (1960).

In these experiments it was necessary to perform simple manipulations on the raw data so that they could be expressed in terms of tension and radius. Fig. 3 will illustrate the method.

The raw data were in terms on x and F. The internal radius a of the equivalent circular vessel is

$$a = \frac{2x + \pi d}{2\pi}.$$

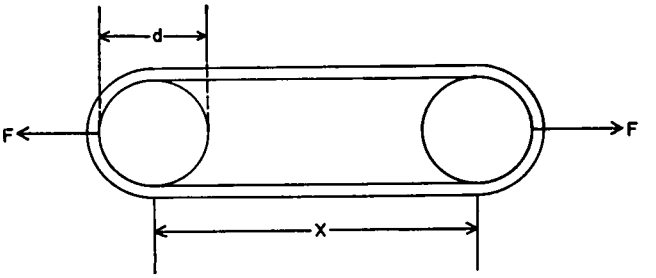

FIGURE 3 Illustration of the method of converting the raw data on length and force to units of radius and tangential tension. $T = \frac{1}{2} F$ and $a = (2x = \pi d)/2\pi$.

The tangential tension contributes twice to the force so that tangential tension equals one-half the measured force.

RESULTS

The time course of typical isometric and isotonic contractions are shown in Figs. 4 and 5. The changes in length and load were made only when the muscle was relaxed. The time course of these contractions is rather slow, even for smooth muscle and limited the number of measurements which could be made.

Isotonic tension-radius plots were measured on 10 vessels and isometric on 10 vessels in the manner described above. The average maximum active force per unit area was 500 g/cm^2 (range 1000–300) for all preparations. The active force was not measured in the isotonic preparations but the value was estimated from the shape of the curves in comparison to the isometric curves. The average radius where the maximum tension occurred in the isometric preparations was 1 mm (range 0.8–1.2). This is near the resting radius of the preparations *in situ*. The positive tension intercept averaged 60 g/cm^2 (range 45–75) in the isotonic preparation and 15 g/cm (range 10–40) in the isometric preparations. The weight of the tissue from which the normalized values are calculated is extremely dependent on the weighing procedure; i.e. blotting pressure, dampness of blotter, etc. These considerations, however, do not affect the accuracy of the tension-radius plots, since these are actual developed force and are not dependent on the weighing procedure. The difficulty only arises in trying to establish average values.

Some attempts were made to circumvent the slowness of the preparation by measuring the entire active radius-tension function while the muscle was maintained in the contracted state. In one series of six experiments the muscle was slowly stretched and then released by an electromechanical device attached to one end. The waveform was triangular and the period was 1 hr. The first half cycle of stretch gave a function similar to the tension-radius function as measured above, however, the release phase of that cycle and all subsequent cycles both stretch and release were very close to the passive curve. If the muscle stimulus was then removed, the

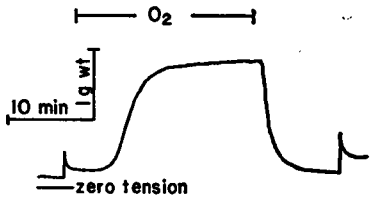

FIGURE 4 Time course of a typical isometric contraction. Period of oxygen stimulation is shown by upper bar. Figure is a tracing from the original record.

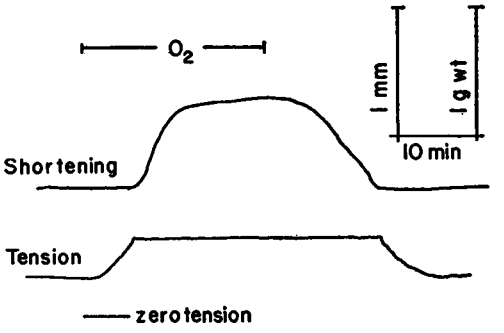

FIGURE 5 Time course of a typical afterloaded isotonic contraction. Upper trace shows shortening as an upward deflection, lower trace shows tension development as an upward deflection. Period of oxygen stimulation shown by upper bar. This figure is a tracing from the original record.

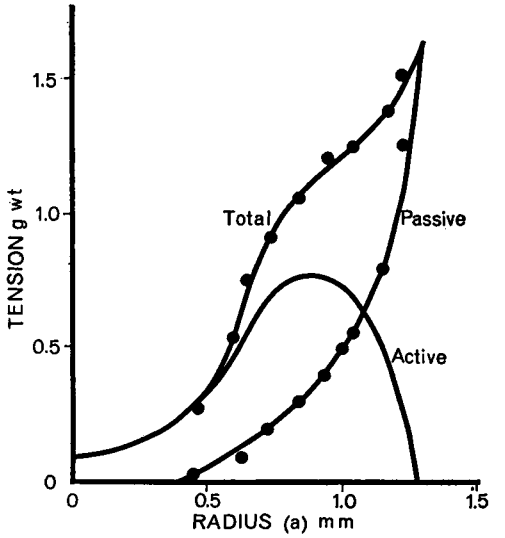

FIGURE 6 Isometric tension-radius diagram measured by the first method described in the text.

muscle could not subsequently be stimulated to develop more than slight forces at any length.

In a second series of four experiments the muscle was stretched without stimulus to a moderately large radius, stimulated, and then released in small increments. The radius-tension functions thus obtained were considerably lower than normal for the first method and positive tension intercepts were not observed.

While both of these attempts at speeding up data collection were unsuccessful

they served to emphasize the care necessary to avoid exposing the muscle to undue mechanical strain.

The complete tension-radius diagrams measured by the first method are shown in Figs. 6 and 7.

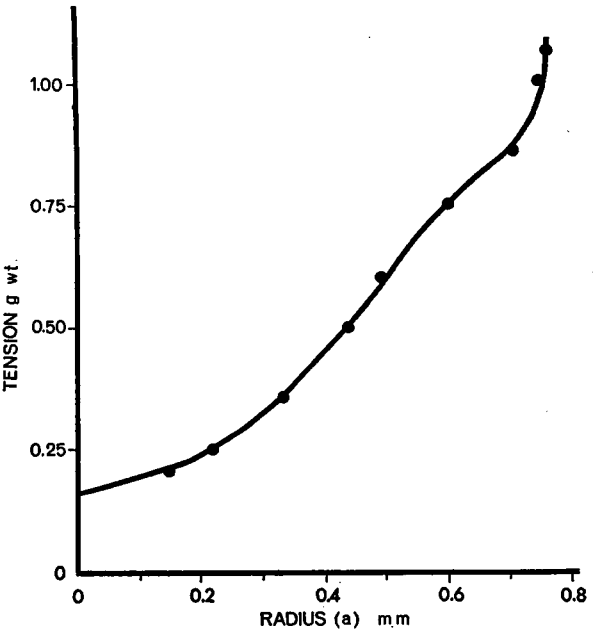

FIGURE 7 Isotonic tension-radius diagram measured by the method described in the text.

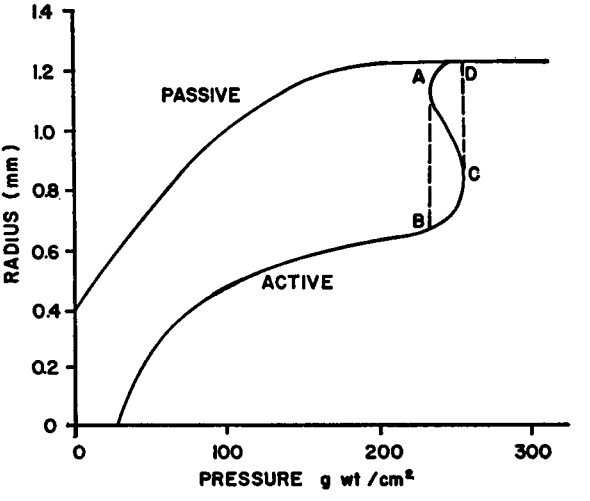

FIGURE 8 Pressure-radius plot derived from Fig. 6 by the method described in the text. *A*, *B*, *C*, and *D* mark the locus of unstable behaviour with decreasing and increasing pressure respectively.

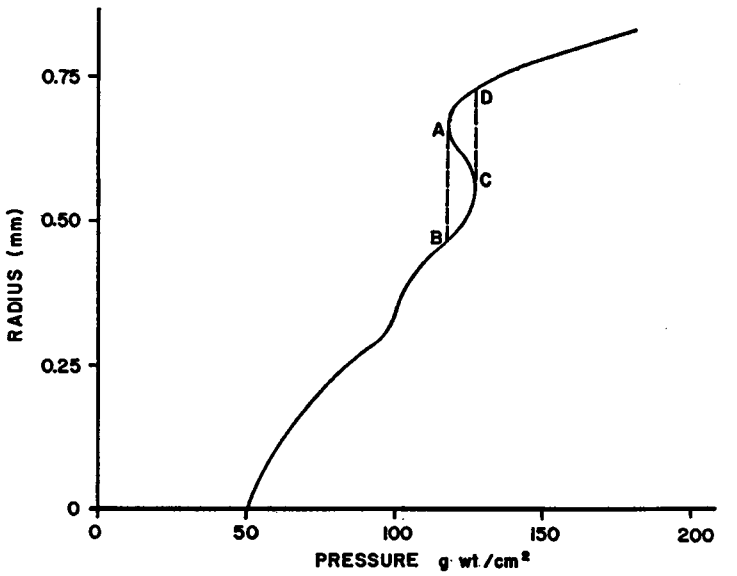

FIGURE 9 Pressure-radius plot derived from Figure 7. *A*, *B*, *C*, and *D*, have the same significance as in Fig. 8.

The smooth curves fitted to the points were drawn by eye using a French curve, therefore, the extrapolations to zero radius are somewhat arbitrary. Using these tension-radius functions as inputs, equation 8 was solved for $F(r)$ and extrapolated to zero force to determine the critical radius c. Using the value of c thus obtained the isobar set for each vessel could be determined and equation 11 was solved graphically from these and the tension-radius diagram. The resulting radius-pressure relationships are shown in Figs. 8 and 9.

The positive pressure at which the internal radius is zero corresponds to the critical closing pressure of Burton. There is, however, no instability of the type present in Burtons model in this region of the curve.

DISCUSSION

The vessels studied were subject to considerable deterioration of performance with stretch. This behavior is not hysteresis in the normal sense because the original behavior (tension development) at short length could not be recovered in time.

This phenomenon was clearly demonstrated in the second and third series of experiments described. This behavior probably arises from the loose wall structure of the ductus which may be subject to considerable permanent reorientation with moderate stretch. Stretching the preparation initially would have made repeated measurements on the same preparation more reproducible, but since knowledge of the absolute level of force development was being sought this procedure was not

adopted. Speden (1960) and others have used prestretching to stabilize smooth muscle preparations and it is likely that in other vascular preparations large amounts of supporting elastic structures make such procedure tolerable. However, in this preparation this was not the case and it was for this reason all the length-tension diagrams were measured in ascending series. The isometric length-tension relationships were obtained by initially stretching the muscle slightly to induce relaxation under zero oxygen tension. It is felt that this treatment renders the isometric data somewhat suspect. However, it is included so that the comparison may be made between active and passive pressure-radius curves on the same vessel. The isotonic data is more reliable but it too is likely to contain a systematic error of lower force at larger radii. The effect would be to make the observed critical closing pressure lower than the true value in the undisturbed vessel.

Since the region of the wall inside the critical radius does not contribute to the balance of forces, the shape of the inner lumen is irrelevant to the question of whether the vessel is closed or not. The shape does enter in, however, if one tries to calculate the hydraulic resistance from the pressure-radius plots in Figs. 7 and 8. The radius in these figures is the radius of a circular lumen. If the wall crenates or buckles as several investigators (Peterson, 1962*a*, 1962*b*; Van Citter, 1966) have indicated, then the effective radius in terms of resistance to flow would be smaller than the value given and the vessel would seem to close earlier, i.e., at higher pressure. The reason for this is that the crenated or buckled vessel approximates a collection of small tubes in parallel. Such a system has a larger hydraulic resistance than a single large tube of equal area. The actual occlusion of course would occur at the same pressure since there is only one geometry for a closed curve of zero area, i.e. a point.

The instability predicted by Burton is not expected from this data. That is the lumen will not occlude suddenly. However, the rate of change of radius with pressure is relatively large near the closing pressure. The regions of negative slope at higher pressures were a consistent phenomenon. The vertical tangents in these regions represent a locus of unstable behavior rather like that which Burton predicted for closing except that in Burtons formulation the reopening pressure (lines *C–D*) is displaced to infinity.

While it is sad to have lost the dramatic closing of the vessel predicted by Burton, we have gained in that these equations predict that the vessel will reopen smoothly from the closed condition when the pressure is raised. In simple terms, this is because the vessel never really closes with respect to the transmission of pressure. The region below the critical radius impedes the movement of fluid, but since it can support no radial shear, it transmits the pressure unimpeded to the rest of the wall elements. The infinite reopening pressure has been a major objection to Burton's original analysis.

The other most common criticism of Burton's analysis is that it omits consideration of the vessel wall thickness (Peterson, 1962*a*, 1962*b*). Burton has derived a

formula which included wall thickness and would also predict a noninfinite reopening pressure since the wall tension does not go to zero as the lumen radius goes to zero. However, Burton states that the isobars do pass through the origin in the same article (Burton 1962), and the point certainly remains confused. While in all likelihood it is true that in a thick-walled vessel the stress varies through the wall, the integral of this stress through the wall does not depend on the wall thickness unless the external pressure is significant.

Most of the trouble in Burton's original analysis was due to an over-idealization of the system. If one is free to define tension as being independent of radius, then, of course, it will not be zero at zero radius. However, such behavior has not been observed for any muscle studied heretofore, and is certainly not true of the preparations in this study. In fact, if one accepts equation 5 as being an accurate model of the vessel wall, the active fibre tension is more strongly dependent on length in the physiological portions of the curve than the passive tension is. However it should be emphasized that the qualitative behavior discussed here is not dependent on the particular form of equation 5. Equation 5 allows the calculation of the critical radius c but if the value of c were miscalculated it would only change the level of pressure at which closure occurs. The phenomenon of smooth closing and reopening follows from a consideration of the fact that the region of the wall below the critical radius does not contribute to the balance of forces in the wall. As stated previously, this relationship is quite independent of the precise constitution of the material of the wall as long as it is ropy.

The point to be made is that the ability of a vessel to close its lumen is predicated on the presence of a relatively thick wall. The wall is not a complication but rather the keystone to closure and any attempts to do away with the wall thickness tend only to confuse the issue.

Equation 11 is very similar to Burton's original formulation of Laplace's law, at least for all radii above the critical radius c. Below the radius c the relationship is even simpler, being a constant. The only difficulty in applying this method is the determination of the slack or critical radius c which can be done using equations 8 and 11 together. All the data based on Burton's original formulation at large radii are still valid, but values based on closing pressure should be reevaluated.

Several previous studies have reported on length-tension relationships for vascular smooth muscle (Speden, 1960; Sparks and Bohr, 1962; Gordon and Nogueria, 1962). However, none of these were done on preparations sufficiently muscular to occlude the lumen on contraction and they all omit critical dimensional data which might allow a partial comparison to this work. A more easily related study is that of Van Citter (1966) who has shown from histological studies on mesenteric vessels which occlude their lumen upon activation that there exists a minimum ratio of wall thickness to lumen diameter in the passive vessel below which the vessels are unable to occlude. This ratio for the vessel Van Citter studied was 1:5. If some known function is substituted for $F(r)$ in equation 5, one can calculate what sort of

wall to lumen ratio would be required to close the vessel against a given pressure. For instance, assuming that the fibers can shorten by 40% and develop a maximum stress of 1 kg wt/cm^2, a vessel with a passive lumen diameter of 2 mm would require a wall to lumen ratio of 1:12 to close against a minimal pressure and a ratio of 1:2.3 to close against a pressure of 100 mm Hg. The ratio for the isometric vessel reported here was 1:6.7 (D = 1.6 mm) and the closing pressure was calculated at 23 mm Hg. The ratio for the isotonic vessel was 1:4 (D = 1.2 mm) and the closing pressure was calculated at 50 mm Hg.

A theoretical modeling study (Crisp, 1968) has been published which ostensibly answers the reopening pressure objection to Burtons model. The answer however takes the form of a perturbation of the radius of the vessel independent of the pressure. Perturbations of this type are physically plausible but since the pressure radius plots are asymptotic to the pressure axis (see Crisp 1968, Fig. 2) the perturbation, formally at least, amounts to a transient increase of the pressure to infinity. If such radial perturbations of the lumen do not occur the closed lumen represents a locus of stability at all pressures up to infinity. This behavior is as stated before due to the membrane approximation and the unrealistic nature of the active tension assumed.

This model in terms of a thick-walled vessel which closes its lumen has two major advantages over earlier models. One, it is no longer necessary to propose any unneed not, have length-tension characteristics identical to those of skeletal muscle. Secondly, since the pressure required to open the vessel lumen is the same as the closing pressure the most troublesome objections to the original theory of Burton is met.[1]

SUMMARY

Tension-radius diagrams have been determined for a vessel consisting primarily of vascular smooth muscle. These relationships together with a new analysis of the physics of the thick-walled vessel predict that this vessel will undergo critical closure at low intravascular pressures. The new relationship is similar to that originally derived by Burton for large radii but for values of the luman radius below a critical value equilibrium tangential tension is independent of radius.

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The author wishes to acknowledge the support and encouragement of Dr. Allan J. Brady and Dr. W. F. H. M. Mommaerts, and the helpful comments and advice of Dr. Victor E. Hall on this problem. The assistance of Mr. Myron O. Schilling and Mr. Charles Dubkin in the design and construction of the equipment was greatly appreciated. The theoretical portion of this work was completed during Dr. McIntyre's tenure as a Postdoctoral Fellow of The Muscular Dystrophy Assoc. of Canada.

Received for publication 29 *August* 1968.

[1] Part of this material has been presented as a brief communication to the 10th Annual Meeting of the Biophysical Society, February 23, 1966, at Boston, Mass.

REFERENCES

BURTON, A. C. 1951. *Amer. J. Physiol.* **164**:319.

BURTON, A. C. 1954. *Physiol. Rev.* **34**:619.

BURTON, A. C. 1962. Handbook of Physiology; Section 2, Circulation. 85–106. Amer. Physiol. Soc. Washington.

CRISP, J. D. C. 1968. *Microvascular Res.* **1**:35.

FUNG, Y. B. 1968. *Appl. Mech. Rev.* **21**:1.

GORDON, D. B., and A. NOGUERIA. 1962. *Circ. Res.* **10**:269.

HOLMES, R. L. 1958. *J. Anat.* **92**:304.

KENNEDY, J. A. and S. T. CLARK. 1941. *Anat. Rec.* **79**:349.

KOVALCIK, V. 1963. *J. Physiol. (London).* **169**:185.

LAMPORT, H. and S. BAEZ. 1962. *Physiol. Rev.* **42**:328.

MCINTYRE, T. W. 1965. Active and passive mechanical properties of vascular smooth muscle. Dissertation. Department of Physiology, U.C.L.A., Los Angeles.

NICHOL, J., F. GIRLING, E. B. JERRARD, and A. C. BURTON. 1951. *Amer. J. Physiol.* **164**:330.

PETERSON, L. H. 1962. *Mod. Concepts Cardiovasc. Disease.* **31**:725.

PETERSON, L. H. 1962. *Physiol. Rev.* **42**:309.

SCHILLING, M. O. 1960. *Rev. Sci. Instr.* **31**:1215.

SPARKS, H. V. and D. F. BOHR, 1962. *Amer. J. Physiol.* **202**:835.

SPEDEN, R. N. 1960. *J. Physiol. (London).* **154**:15.

VAN CITTERS, R. L. 1966. *Circ. Res.* **18**:199.