PHASIC VARIATIONS IN PERIPHERAL CORONARY RESISTANCE AND THEIR DETERMINANTS

DONALD E. GREGG, HAROLD D. GREEN AND CARL J. WIGGERS

From the Department of Physiology, Western Reserve University Medical School, Cleveland, O.

Received for publication March 22, 1935

Information regarding the successive changes of resistance in the coronary branches and their determinants is of paramount importance both in understanding the phasic changes of coronary flow and in interpreting the actions of drugs upon the intact coronary circulation. It seemed that a study of the pressure pulse from the peripheral end of a coronary vessel (peripheral coronary pressure—P.C.P.) should supply this information.

This report deals with a description of such pulses recorded by a calibrated optical manometer together with an analysis of their phasic variations and of their reliability in appraising the variations of peripheral coronary resistance under natural conditions.

PROCEDURE. In a first series of experiments aortic and peripheral coronary pressures were simultaneously recorded by two optical manometers (Wiggers pattern). The cannula of the coronary manometer—modified as illustrated in figure 1A—was inserted into the peripheral end of the ligated descending ramus as indicated in figure 1A, the precautions emphasized by Wiggers and Cotton (1933) being observed. Through the lateral connection and stopcock (a) the peripheral coronary vessel was perfused with Locke’s solution, except when records were being taken. Experience had taught us that by this expedient coagulation in the cannula tip could be prevented and the danger of the heart failing through fibrillation or hypodynamic action could generally be averted.

During the course of such studies the discovery was made by Tennant and Wiggers (1935) that an area so perfused extends during systole instead of shortening. Since replacement of a normal systolic shortening by an extension might conceivably alter the peripheral coronary resistance changes, a second method for recording P.C.P. was devised by which normal contractions were retained in the area studied. The procedure consisted in isolating the anterior descendens or the circumflex ramus and also a suitable side branch and in tying the coronary cannula into the

1 The expenses of this investigation were defrayed from a grant by the Ella Sachs Plotz Foundation.
latter, as illustrated in figure 1B. The normal blood supply to the area studied was thus kept intact, except while taking records, when the main vessel was clamped centrally to the side branch. Coagulation was prevented in the cannula by flushing it repeatedly with Locke's solution to which heparin had been added. Myographic records showed that such admixture of heparinized Locke's solution had no effect on contractions in the areas studied. By compressing the main branch for several minutes, records could also be obtained when the area supplied did not shorten. By releasing the clamp and restoring the blood supply, normal contractions returned in the area affected as described by Tennant and Wiggers (1935).

In order to improve the "figure of merit" of the manometer equipped with a relatively small cannula tip, a very tense rubber membrane was used. The resulting decrease in sensitivity was compensated for by moving the photokymograph away to a distance of 2.6 meters. Adequate intensity of beams was insured by using small plano-convex mirrors flooded by light from a projection bulb, as suggested by Hamilton, Brewer and Brotman (1934).

The contour of peripheral coronary pressure pulses. Typical records from a heart in which the zone determining peripheral pressure changes was presumably extending during systole (method 1) are reproduced in figure 2. The form of the aortic pressure curves and the ordinate values derived from application of a calibration-scale attest to the existence of good dynamic conditions. Record A was obtained shortly after cannulation of the peripheral coronary branch. Vertical intercepts facilitate comparison of the phasic relations of the two pressure pulses. The curves show that 0.046 second before the steep rise of aortic pressure, i.e., probably coincident with the isometric rise of intraventricular pressure, the peripheral coronary curve rises, slowly at first (A–B), then brusquely (B–C). This rise continues more gradually into the period occupied by the steep
Fig. 2. Records illustrating time relations, contour and magnitude of peripheral coronary pressures. A, normal control; B, during clamping left circumflex ramus; C, after release of same; and D, during clamping of right coronary artery. A.B., aortic base line; A.P., aortic pressure pulse; C.P., peripheral coronary pressure; C.B., coronary base line. Time, 0.02 second. Discussion in text (expt. DD-1/5–8).
Fig. 3. Comparison of P.C.P. curves from anterior descendens ramus (A) when area extended during systole, and (B) when same area shortened. (C) record from left circumflex when area contracted. M, myogram; X, time of clamping main coronary; other lettering as in figure 2 (expt. DD-32/6-7; DD-36/10).
rise of aortic pressure \((C-D)\), then mounts as a gradually rising plateau almost but not quite to the end of systole \((E)\). During protodiastole \((E-F)\), the curve starts to decline. At first it falls rapidly, then more slowly during the isometric relaxation phase \((F-G)\). At the time ventricular inflow starts \((G)\), the fall in pressure is practically completed.

The time relations and general features of the rise and fall correspond to changes of pressure within the left ventricle, but the gradually rising plateau differs essentially from the rounded summit of intraventricular pressure which may be judged from the aortic pressure summit. With minor differences these general characteristics were found in all records. In some instances the abrupt initial rise \((B-C)\) extended through the period of rising aortic pressure \((C-D)\). The gradient of the systolic plateau also varied in different experiments.

Examples of records in which the area was stretched \((A)\) and in which it was shortening during systole \((B)\), (method 2), are shown in figure 3. Record A was taken after the main branch of the ramus descendens had been clamped for 3 minutes, i.e., after sufficient time had elapsed to cause marked extension of the area supplied.\(^2\) This extension is demonstrated by the myographic record which descends abruptly during isometric contraction \((a-b)\) and rises with isometric relaxation \((d-f)\). The peripheral coronary pressure pulses \((\text{beats } 2, 3)\) show essentially the same features as those described above. Immediately after taking this record the coronary clamp was removed and the area allowed to recover. Record B in which the myogram now shows a continuous shortening during ejection \((c-d-e)\) and slightly beyond it, was then recorded.

The coronary curve of this latter record starts with two beats representing lateral coronary pressure. They serve the purpose of assuring adequacy of the manometer and proper alignment between the manometer and artery. At \(X\) the main ramus was clamped abruptly and from this point on peripheral pressure changes were recorded.

The corresponding beats marked 2 or 3 in records A and B are very similar, the only difference noted upon close examination of record B being 1, a somewhat steeper rise of the plateau continuing to the very end of systole; 2, a somewhat slower gradient of decline during isometric relaxation; 3, a higher pressure maximum during systole, and 4, a trifling increase in diastolic pressure. If we accept such differences as significant it might be inferred that the existence of local contractile forces tends somewhat to augment the pressure rise during the ejection phase and to retard the decline of pressure during early diastole. In some experiments however even such differences were not apparent, while in others the initial

\(^2\) Just before taking the record the vessel was distended by perfusion with Locke’s solution through the side cannula and the point \(X\) on the record denotes the moment when it was stopped.
sharp elevation of pressure appeared to shift from the isometric period to the time that the aortic pressure rose. It should be noted however that in some experiments of our first series a steep rising plateau was present. It is significant that in all experiments the rise of coronary pressure \((a-b)\) definitely preceded shortening as inscribed by the myogram at \(c\) and that the decline of peripheral coronary pressure definitely preceded the actual lengthening of the muscle \((e)\) and began coincidentally with the incisura \((d)\), i.e., with the fall of intraventricular pressure.

Record C of figure 3 is added without further description as evidence that curves similar in contour can be recorded from the peripheral end of the circumflex ramus (method 2). Although a myogram could not be conveniently recorded there is every reason to believe that the region affected continued to shorten, for no compression of the vessel had been made previous to this test.

The determinants of phasic variations in peripheral coronary pressure. The systolic increase in peripheral coronary pressure may be due, a, to increased intramural or intraventricular tension; b, to compression of intramural vessels by shortening and thickening of muscle elements, or c, to transmission of pressure from collateral vessels.

In favor of the concept that tension change is the predominant factor are the discoveries 1, that the sharp rise and fall of peripheral coronary pressure coincide respectively with the steepest rise and fall of intraventricular pressure, but are not synchronous with the onset of shortening or lengthening recorded myographically, and 2, that as long as intraventricular pressures do not alter, the contour of the curves does not differ essentially regardless of whether the region shortens or lengthens during systole. The fact that the systolic maximum is less when the area supplied lengthens during systole (as in ischemia) can be interpreted to mean either that muscle shortening (and thickening) is normally of supplementary assistance or that stretching increases the capacity of the coronary vessels sufficiently to prevent a full development of systolic pressure (see below).

Before we may conclude that tension changes are chiefly concerned and that length changes play at most a subsidiary rôle, it is necessary to evaluate the part that pressure transmitted through collateral anastomoses with other branches may play. The magnitude of the peripheral collateral circulation in the normal heart is still unsettled, despite extensive anatomical and experimental studies. Experimental studies can easily be cited in favor of either an abundant or a negligible collateral circulation. For instance, if mean pressures are simultaneously recorded from a peripheral coronary branch, and from the aorta, the former is approximately one-fifth that in the aorta; and if aortic pressures are caused to rise by any of several methods this proportionality is roughly maintained. We have
studied such relationships extensively and have even attempted their use in evaluating the effect of drugs on the collateral supply of blood to infarcted areas. We slowly came to realize, however, that it is hazardous to conclude that such correspondence denotes a cause and effect relation, for the dynamics of the left ventricle is modified whenever aortic pressure alters (Wiggers, 1928). That increased ventricular contraction with its concordant increase of the intraventricular pressure maximum is indeed the dominant factor is shown in the record of figure 4, in which aortic and peripheral coronary pressures were recorded while the aorta was being compressed. The rise affects chiefly coronary systolic pressure; diastolic pressure is raised only to an insignificant extent. More important, however, is the fact that the higher systolic pressure occurs chiefly through a greater initial rise which precedes the elevation of aortic pressure, hence

![Figure 4](http://ajplegacy.physiology.org/Downloadedfrom)

**Fig. 4.** Aortic (upper) and P.C.P. (lower) showing effect of aortic compression. Discussion in text (expt. DD-5).

the change could not be assigned to transmission of pressure from collateral branches. Opposed to the idea that a significant collateral supply exists are a, the recent observation of Tennant and Wiggers (1935) that recognizable contractions in the ischemic area discontinue approximately within a minute after occluding a main branch, and b, our own observations that the flow of blood from the peripheral end of a major coronary vessel is extremely small. In the experience of workers in this laboratory, only an occasional drop flows from a cannula in the peripheral end of the anterior ramus descendens of the dog, the total flow per minute being less than 1 cc. Flow rates which even approach those reported by Anrep and Häusler (1928) have never been encountered. These must have been recorded from a hound with unusually developed collateral circuits.

Our analysis of optical tracings (e.g., fig. 2A) precludes attributing the rise of peripheral coronary pressure prior to ejection (A–C) to trans-
mission of pressure from collaterals. The possibility does exist however that the rising systolic plateau (D-E) may be due to such a transfer of collateral pressure. The fact that this slope increases both when the areas contract and when aortic pressures mount (fig. 4) might be cited to support such a possibility.

More direct evidence on these points was obtained by studying changes in P.C.P. in the anterior ramus descendens following additional temporary ligation of the left circumflex and/or right coronary branches. Such studies were complicated by immediate changes in contraction of the ventricles and by the rapid development of ventricular fibrillation. Despite such difficulties and numerous expected failures, successful results were obtained in 5 dogs. The records of figure 2 illustrate the results of one such experiment. Record A represents a control which has already been analyzed. Without disturbing the manometers, the left circumflex branch was abruptly occluded by application of a special clamp. Record B was taken as quickly as possible thereafter. The aortic pressure curve displays typical effects of occlusion described by Orias (1932, 1934), among them the relatively small fall in aortic blood pressures and the marked reduction in duration of systolic ejection while the heart cycle remains constant. The coronary diastolic pressure decreased 3 mm. and systolic pressure, 6 mm. After occlusion of less than a minute the clamp on the left circumflex ramus was released and within another minute curve C was taken. It is practically identical with that of curve A as regards contour, amplitude and time relations. Then, the right coronary was similarly occluded near its origin and curve D taken. It shows no significant changes of any sort.

These and many similar tests showed clearly that compression of the right coronary artery is without effect upon peripheral pressure in the ramus descendens anterior; occlusion of the left circumflex branch on the other hand reduces coronary systolic pressure and modifies the form of the curve. The bulk of evidence distinctly favors the view that the changes noted result chiefly and perhaps entirely from altered contraction of the left ventricle, for 1, the lowered coronary systolic pressure (record B) is chiefly due to a smaller initial rise which transpires before any transmission of collateral pressure could have taken place, and 2, the systolic plateau shows an actual increase in the rate of rise, not a decrease, as would be expected if a collateral transfer of pressure had been abrogated.

The slightly rising plateau therefore remains difficult to interpret. The possibility must still be considered that it represents a slight transfer of pressure directly from the ventricular cavities. Such an interpretation would give a function to the communicating channels described by Wearn et al. (1933) and would account for the appearance in capillaries of particulate matter injected into the ventricles when the coronaries are perfused.
from an extraneous source (Bohning, Joehim and Katz, 1933), without necessarily demonstrating the efficiency of such a circulation.

On the basis of such studies the conclusions are reached that the transfer of pressure from collateral vessels plays no significant part in determining the contour or magnitude of peripheral coronary pressure pulses and that the systolic increase in peripheral coronary pressure is chiefly due to muscle tension rather than to changes in muscle length.

Peripheral coronary pressure variations and the appraisal of peripheral coronary resistance. Numerical values for the P.C.P. changes expressed in millimeters mercury and referred to zero at the aortic cannula tip are inscribed directly on curves presented in our illustrations. They indicate the order of magnitude generally found, although considerable difference occurs, particularly in the systolic maximum pressure. Such values doubtless represent the actual maximal pressures developed peripherally to an occlusion under given dynamic conditions. If, however, they also indicate the extreme magnitude of the systolic increase in resistance under normal conditions, then the systolic pressure-difference in the large coronary vessels is great enough to cause a much larger systolic flow than observations by flow-recorders have indicated (Wiggers and Cotton, 1933). A suspicion that such inferences are questionable was aroused by the observations of Anrep and Saalfeld (1933) that when auto-perfused coronary vessels are briefly clamped during systole, the peripheral pressure holds at far higher levels than indicated by our figures. While we have found by repetition of their experiments that the holding level is always distinctly below aortic systolic pressure, it greatly exceeds the pressure maxima indicated in direct P.C.P. curves. Confirmatory evidence is given in the observations that after sudden compression of a coronary branch, the peripheral systolic pressure developed in subsequent beats depends upon the diastolic level from which they start. Thus in the record of figure 3 B, the systolic height decreases progressively in beats 1, 2 and 3. Observations in other experiments showed that even a greater systolic elevation of the curve occurred in still earlier beats, as, for example, the one sketched upon the record. If such beats are enlarged by projection and then redrawn to identical coördinates, their form is found to be unchanged. Such results clearly show that the degree to which the coronary vessels and their branches are filled affects the magnitude of the pressure increment during systole under identical dynamic conditions of cardiac action, but does not alter their form.

The conclusion logically follows that optically recorded curves of P.C.P. picture the sequential changes in peripheral coronary resistance correctly as regards time relations and relative magnitude, but they cannot be used quantitatively to appraise the maximum systolic resistance under natural conditions.
We are able to interpret this entirely unforeseen situation in only one way, viz., by postulating a disproportion between the systolic back thrust of blood from the minute vessels and the elastic accommodative capacity of the coronary system involved.

Circumstantial experimental evidence supports this view. The volume-elasticity relations at internal coronary pressures from 20 to 180 mm. Hg were studied immediately after our experiments, in 14 hearts. The method first used consisted in blocking the capillary bed supplied by the ramus descendens anterior by perfusion with a dilute suspension of lycopodium. The vessel was connected to a horizontal micropipette and manometer, and volume-pressure relations were determined. After such treatment blockage was rarely complete for aqueous fluids, but when the vessels and apparatus were filled with mercury, pressures generally held.

Volume-pressure relations of the anterior descending ramus and its branches in hearts weighing about 100 to 150 grams are shown by a composite curve in figure 5. Examination reveals that a volume increase of about 0.12 cc. is required to produce a pressure rise from 20 to 100 mm. (line a). Similar tests with the optical manometers used showed that introduction of 0.0035 cc. sufficed to cause a similar rise in pressure. Applying such figures it becomes apparent that a pressure of 100 mm.

Fig. 5. Plot showing volume-pressure relationships in ramus descendens anterior. Discussion in text.
could only develop in the occluded coronary vessels provided the volume increased at least 0.12 cc. and that registration of the full change by our manometer would require only a trifle more, i.e., a total volume of 0.1235 cc. The only source for this added blood in occluded coronary territory would be by squeezing blood back from minute vessels during systole; a supply from collaterals can at once be eliminated for the major elevation of pressure precedes the rise of aortic pressure. By drawing on the curve of figure 5 vertical lines, 1, 2, 3, the lengths of which correspond to the pressure increases shown in similarly designated beats of figure 3, it becomes apparent that the capacity change and presumably the systolic backflow is of the order of only 0.03 cc.; further that only slight differences in diastolic coronary pressures (i.e., distention) are required to increase the magnitude of the backflow denoted successively by lines 3, 2 and 1. It thus becomes quite possible that in this experiment sufficient backflow to elevate pressures to 90 mm. could have occurred only when the coronary system was distended by considerably higher diastolic pressures (circa 45 mm.). This hypothetical condition is illustrated by the vertical line b.

Observations such as these suggest that, as far as the anterior ramus descendens territory of the dog is concerned, the systolic backflow is much less than generally believed. When a peripheral coronary vessel is perfused with Locke's solution at approximately their diastolic pressures (circa 20 mm.) jets of red blood can be seen to enter the cannula during each systole and to leave during each diastole. This phenomenon which attracts the attention of all workers leaves an exaggerated impression of backflow for it must be remembered that blood diffuses rapidly into adjacent saline and rarely shoots much beyond the tip of a cannula, the total capacity of which is only 0.1 cc. Experimental estimates by means of a flow recorder still to be described indicate an actual to and fro movement of about 0.04 cc.

**SUMMARY AND CONCLUSIONS**

In order to study the phasic changes in peripheral coronary resistance qualitatively and quantitatively, pressure changes in a peripheral coronary branch were recorded optically by two procedures.

Such records indicate that our current conceptions regarding the time relations, character and magnitude of peripheral coronary resistance require some revision:

1. Normally, the peripheral coronary pressure (P.C.P.) increases quickly during isometric contraction and the first moments of ejection, rises more gradually to a summit during the shortening phase, decreases abruptly during isometric relaxation and is influenced but little by subsequent lengthening of ventricular muscle.

2. Such time relations together with the demonstrations a, that P.C.P.
curves are not materially affected when the regions involved extend instead of shorten (ischemia), and b, that at constant diastolic pressures, systolic coronary pressure increases proportionately to systolic aortic pressure, when the latter rises, indicate that intramural and intraventricular tension rather than muscle fiber length predominantly determines the resistance.

3. The fact that the systolic maximum pressure is reduced somewhat when the involved muscle-area extends instead of shortens can be interpreted to mean either that muscle shortening is normally of supplementary assistance or that stretching increases the capacity of the coronary branches sufficiently to prevent full development of systolic pressure.

4. Peripheral coronary resistance is not affected to any discoverable extent by transmission of pressure from collateral branches because a, the magnitude of flow from an open peripheral ramus is very small; b, the steep and major rise of P.C.P. occurs prior to development of maximum aortic pressure, and c, clamping of the right or/and left circumflex rami produce no phasic changes in resistance and only such deviations in magnitude as can be better explained by concurrent changes in the dynamics of ventricular contraction.

5. In beats equivalent as regards contractile force, the systolic pressure maximum reached depends upon the diastolic pressure level from which a beat starts, i.e., upon the degree of coronary filling. Volume-elasticity studies of the coronary system, interpreted in conjunction with pressure changes and flow determinations, strongly suggest that the systolic backflow is of the order of 0.03 cc. which is considerably less than usually stated. Since this backflow is less than that required for development of the total pressure of which the myocardium is capable, pressure curves recorded from a peripheral ramus do not allow an appraisal of the maximum resistance developed under natural conditions of coronary distention.

The facts presented are of fundamental importance in understanding phasic changes of coronary flow and in interpreting the actions of drugs upon the intact coronary circulation.

REFERENCES

ANREP, G. V. AND E. V. SAALFELD. J. Physiol. 79: 317, 1933.
BOHNING, A., K. JOCHIM AND L. N. KATZ. This Journal 106: 183, 1933.
ORIAS, O. This Journal 100: 629, 1932.
REV. SOC. ARG. DE BIOL. 10: 12, 1934.
TENNANT, R. AND C. J. WIGGERS. This Journal (This volume, p. 351).
WIGGERS, C. J. AND F. S. COTTON. This Journal 106: 9, 507, 1933.