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THE ELECTROCARDIOGRAPHIC EVIDENCE OF LOCAL VENTRICULAR ISCHEMIA (*)

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INTRODUCTORY REMARKS

The comparison of electrocardiographic changes with necropsy findings has helped establish much of the foundation of modern electrocardiographic interpretation. Nevertheless, when the laws which define the flow of electric currents are properly applied to the electrical effects of the heartbeat, the results are powerful concepts of proven value [1, 2] in the interpretation of the electrocardicgram. Since it appears that cardiac muscle in the ischemic electrical state is disturbed physiologically rather than pathologically, considerable reliance must be placed upon these concepts when seeking a solution of the present problem. We are particularly indebted to the many contributions of Dr. Frank N. Wilson and his associates of the University of Michigan for many of the fundamental concepts which have made the present studies possible.

THEORETICAL CONSIDERATIONS

Deeply inverted T-waves which reach a sharp voltage peak late in electrical systole were first observed by Smith [3] in limb leads which

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were obtained from dogs following ligation of a coronary artery. Several years later the distinctive character of the "coronary T-wave" was described by Pardee [4] as occurring in the limb leads of human subjects who were suffering from disease of the coronary arteries. T-waves of the kind specified were described still later by Wilson et al. [5] as occurring regularly in unipolar direct leads which were recorded from dog by placing the exploring electrode upon the heart muscle at the boundary of an experimental infarct. For the first time, the distinctive character of the deflection was ascribed by these workers to a local alteration in the time course of the recovery process.

A satisfactory explanation of the widely recognized phases [6] of the sequence of QRS [7], RS-T and T [2] changes which characterize the course of myocardial infarction has been offered in accordance with the dictates [1] of the membrane theory. Certain of the principles are fundamental to a further extension of the theory which incorporates the problem of local ventricular ischemia. The extended arguments have been presented elsewhere [2] and will not require a detailed consideration at this time.

The source-sink distribution of accession (activation), of regression (recovery), of muscle in the ischemic electrical state, and of muscle in the injured electrical state is lamellar. In the case of accession, the rate of change of polarization at a point is sufficiently rapid for practical purposes to be regarded as instantaneous [1] Consequently, the accession process may, at any instant, he regarded as a single uniform lamella of constant electrical moment which separates muscle in the resting from muscle in the excited electrical state. In general, the accession lamella will be one of three kinds, first, second, or third (Fig. 1). A lamella of the first kind is defined as closed and, in the case of a diffuse ground, produces no potential at an outside field point. In the case of a volume conductor of limited extent, an accession lamella of the first kind produces no outside potential difference. The potential at any inside point is everywhere equal in magnitude and negative in sense. An accession lamella of the second kind is defined as bounded by one closed curve. An accession lamella of the third kind is defined as bounded by more than one closed curve. The bounding curves necessarily lie at the surface of the muscle mass and their orientation at any instant is determined by the order of accession of the muscle units at the epicardial and the endocardial surfaces. The potential at an outside or inside point is determined, in a proportional way, by the orientation of the bounding curves. The order of accession of muscle units which lie between the ventricular surfaces determines at any instant the configuration of the surface

of the accession lamella, a property of which the potential is entirely independent.

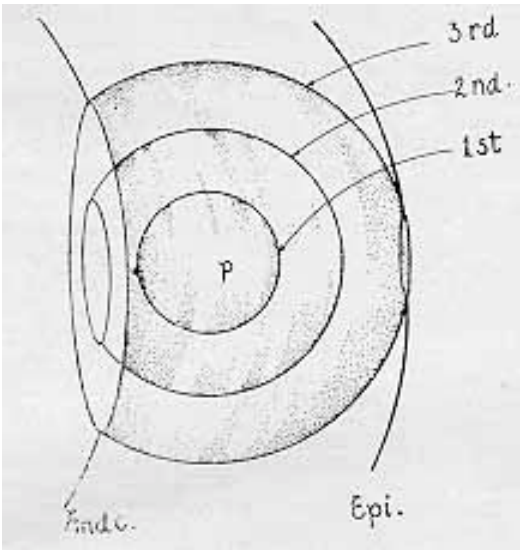


Fig. 1 - If it is supposed that an extrasystole develops from a point of stimulation p which is located within the free wall of the left ventricule somewhat nearer to the endocardial than to the epicardial surface, the figure shows the accession lamella at three successive instants of time where it a forms a lamella of the first, second, and third kind, respectively. The superjacent electrode of a unipolar lead will record a brief R and a broad S deflection. The figure may also be used to illustrate a regression wave in the process of vanishing at p. The lamella of the third kind forms the tail of the wave. The final positive trace of T will be recorded at about the time at which the tail of the wave reaches the position occupied by the lamella of the second kind. If the figure is used to illustrate a local distribution of injury, it is an example of the injury-against-the-rule for the aggregation of bounding curves is greater at the endocardial, than at the epicardial, surface. See text.

In the case of regression, the relatively greater confines of the regression wave may, at any instant, be divided into lamellae of the first. second, and (or) third kind (Fig. 1). Throughout any regression lamella the change of polarization (which determines its intensity) is everywhere the same. Regression lamellae of the first kind aye defined as closed and, in the case of a diffuse ground, make no contribution to the potential at an outside point. In the case of a volume

conductor of limited extent, regression lamellae of the first kind produce no outside potential difference. The potential contribution at any inside point from regression lamellae which are closed is everywhere equal in magnitude and positive in sense. Regression lamellae of the second kind and of the third kind possesses boundaries which form all aggregation of closed curves that is necessarily located upon the ventricular surfaces. The regression potential due to lamellae of the second kind and lamellae of the third kind is reckoned, in a proportional way, directly from the aggregation of bounding curves. At any instant, the orientation of the bounding curves depends only upon the order of regression of muscle units at the ventricular surfaces and not at all upon the order of regression of units between these surfaces. Consequently, the regression potential which determines the form of T depends only upon the order of regression of the surface units. The order of regression of the surface units depends, in turn, upon two, factors, the order of accession of the surface units and the effective duration of their excited electrical state. Alterations in the form of T due to local alterations in the effective duration of the excited electrical state are called primary T-wave changes. [8,9] Alterations in the form of T due to alterations in the order of accession (or in the form of QRS) are called secondary T-wave changes. [9]

Muscle units which are ischemic are characterized by an abnormal prolongation of the effective duration of the excited electrical state. [2] It is reasonable, therefore, to assume that the physiological change in muscle units at the boundary of an infarct is a consequence of local ischemia. The form of T which is observed in the unipolar direct leads that are recorded with the exploring electrode placed superjacent to the ischemic region is accounted for by a relative delay in regression at the epicardial, as compared with the time of regression at the neighboring epicardial and endocardial, surfaces. With a gradual improvement of the collateral circulation of the ischemic region, the ischemia and its associated primary T-wave changes vanish. [10] If the specified T-wave change is defined as evidence of first degree ischemia, then a second or more intense degree of ischemia, which we shall call injury, might quite naturally be expected to produce not only a local delay in the effective duration of the excited electrical state but a subnormal change of polarization oil regression of the injured region. An electrical event of this kind is necessarily followed by a flow during diastole of a current of injury. The distribution of the injured zone is circumjacent to the central dead zone of the infarcted region. [11] For analytical purposes the injured zone may be divided arbitrarily into lamellae in such a manner that throughout any given lamella the subnormal change of polarization on regression is everywhere the same. If at any instant during diastole line are drawn outward from the dead zone, through the injured zone, to-

ward the ischemic zone, in such a manner that they traverse each encountered lamella in the direction of its outward drawn normal, the direction of these lines defines the direction of the maximum space rate of change (increase) of intensity of polarization. There is every reason to suppose that accession invades the injured (and of course the ischemic) zone. Consequently, the injury current which flows during diastole temporarily reverses its direction of flow during systole. If the exploring electrode of a direct or semidirect unipolar lead is placed superjacent to the epicardial surface of the injured region, the injury effects recorded are necessarily one of two possible kinds. If the aggregation of closed curves which bounds the open injury lamellae is greater at the epicardial than at the neighboring endocardial surface, the diastolic base line will be displaced downward and the RS-T junction will be displaced upward. This is usually the case for local ventricular injury which results from local impairment of coronary flow. The local distribution of injury is greater at the epicardial, than at the neighboring endocardial surface, and is conveniently referred to as *injury-with-the-rule* (Fig. 4). When the aggragation of bounding curves is greater at the endocardial than at the neighboring epicardial surface (Fig. 1), a lead of the kind specified will show an upward displacement of the diastolic base line and a downward displacement of the RS-T junction. Insofar as the authors are aware, the latter distribution of local injury has not been encountered in experiments on animals following ligation of a coronary artery. We believe, however, that we have observed this type of local injury in man and we shall refer to it as *injury-against-the-rule.*

When the distribution of an injured zone is known, it is an easy matter to predict the associated limb lead changes. The diastolic base line displacements are neglected since they are not detectable in the ordinary clinical record. The entire interventricular septum is regarded as a complement of the free wall of the left ventricle, thereby neglecting the relatively unimportant free wall of the right ventricle. This simplification is not permissable when dealing with the injured regions subjacent to pericarditis. In the case of injury-with-the-rule, the direction of the axis of injury is that of a line drawn from the center of the left ventricle toward the center or centroid of the injured region. In the case of injury-against-the-rule, the direction of this axis of injury is that of a line drawn from the center or centroid of the injured region toward the center of the left ventricle. Inasmuch as pericarditis tends to involve the epicardial and not the endocardial surface of the ventricles, the associated type of injury is always with-the-rule. Moreover, when dealing with pericarditis, the center of the ventricular muscle is used instead of the center of the left ventricle. Having determined in this manner the direction of the axis of injury of arbitrary length, the axis is translated into the triaxial reference

system. Its projections upon the reference axes define the directions of the RS-T junction displacements in the limb leads. [11]

If the injured electrical state is unstable, the muscle units which support it must either die or pass into the ischemic electrical state during the course of recovery. If the majority of units in the injured electrical state die, the disappearance of the injured zone will contribute chiefly to those permanent QRS changes which characterize the dead zone of myocardial infarction. If the majority or all of units in the injured electrical state recover by passing into the ischemic electrical state, the QRS changes that are characteristic of the damage will diminish or completely disappear. Concurrently, the transition of muscle units from the injured into the ischemic electrical state will create a greater zone of ischemia about the dead zone of the infarct. In the absence of muscle death, the transition specified will simply revert to a larger zone of local ventricular ischemia. The disappearance of the electrocardiographic effects of injury should, therefore, enhance the effects of local ischemia.

At the foregoing stage of elaboration of a theory of ischemia and injury, it occurred to the senior author that, since cardiac muscle traverses the ischemic state while passing from the injured into the normal electrical state, it should at least be probable that cardiac muscle traverse the ischemic state when passing from the normal into the injured electrical state. At this time, the literature failed to reveal any description of electrocardiographic changes which might support the foregoing argument. On the contrary, the idea prevailed that pronounced RS-T junction displacements were the first electrocardiographic changes which followed sudden occlusion of a coronary artery. In one experimental study [12] early RS-T junction displacements were shown but the trends of the pattern were neither illustrated nor described in sufficient detail to interpret the associated T-wave inversions. In the meantime, however, several clinical observations [10,11] seemed to lend a measure of support to the foregoing argument. Subsequently, we have been able to offer what is regarded as strong support for the hypothesis and to extend further the solution of the present problem.

EXPERIMENTAL FINDINGS

The experimental findings of acute local ventricular ischemia and of injury have been studied recently in the dog. [13,14,15,16] Unipolar direct leads ordinarily yield patterns of three kinds when a coronary artery is occluded temporarily. The majority of these patterns are of what we have called the positive-T or the negative-T variety. They are so named according as the sense of T appears positive or negative in the control curve which is recorded before occlusion and after arterial dissection.

As a typical pattern unfolds it displays the so-called *ischemia phase* which occupies the first thirty seconds after occlusion and consists only of characteristic primary T-wave changes. In the positive-T pattern, the change is a gradual inversion of T (Fig. 2) and, in the

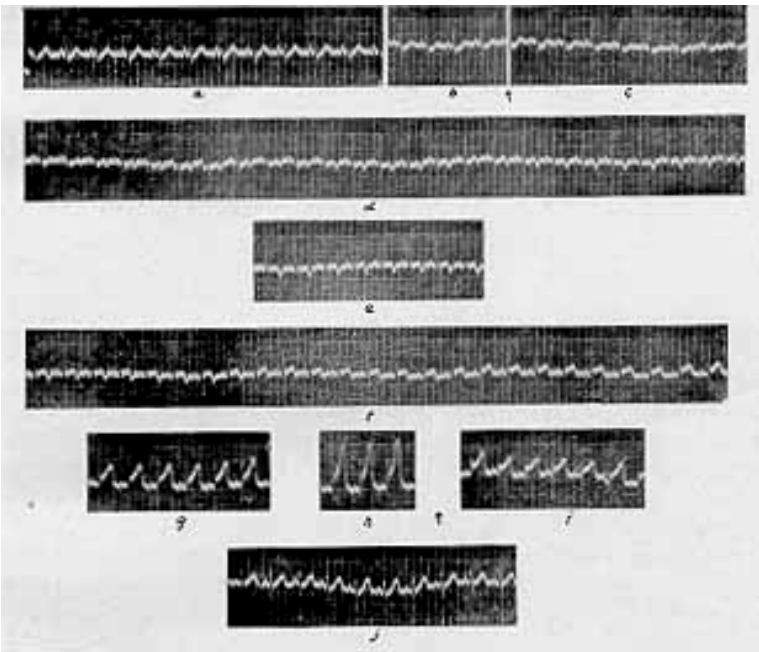
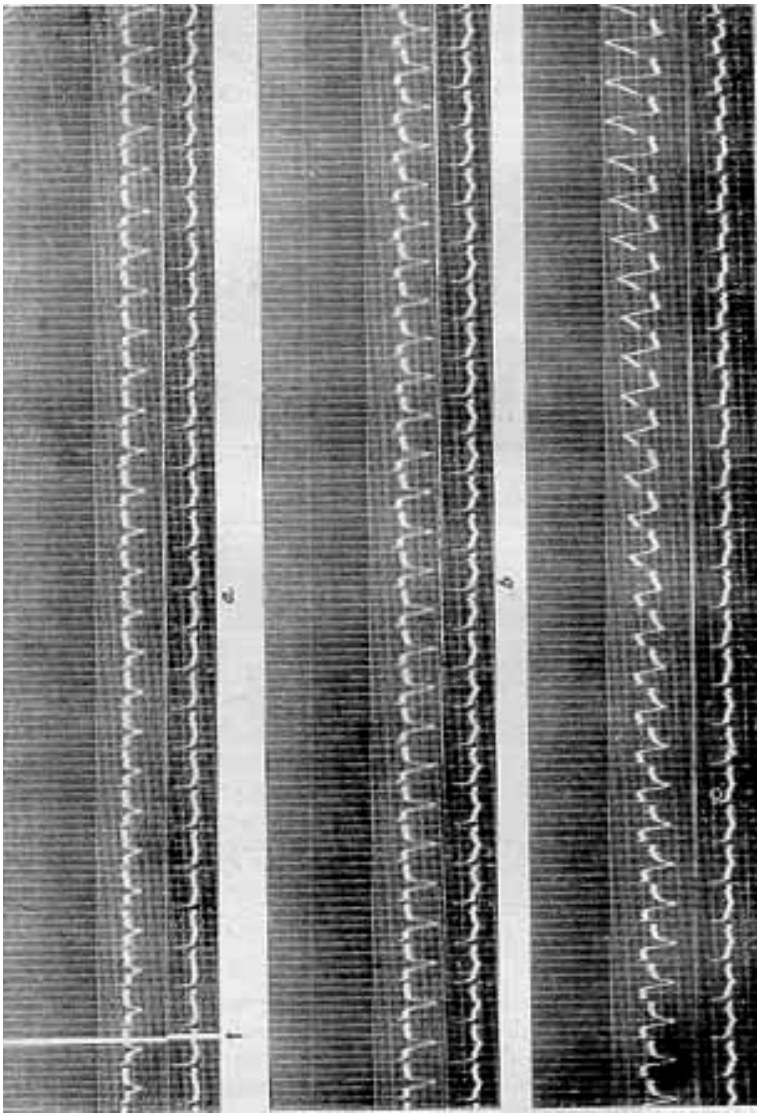


Fig. 2 - The positive-T pattern, a and b are controls before experimental occlusion in dog. c, d, and e show the ischemia phase. f, g, and h show the phase. Occlusion ended between h and i. j shows the return to the control form. The occlusion lasted for ninety seconds. The beginning and end of occlusion are indicated by the arrows. (See Fig. 1 of Reference 13).

negative-T pattern, the inverted T shows a gradual increase of amplitude (Fig. 3). During the next fifteen seconds both patterns undergo a transition into the so-called injury *phase* in which the diastolic base line invariably becomes displaced downward and, concurrently, the RS-T junction ordinarily becomes displaced upward. As the separation of the displaced portions of the curve increases, the T displays a “waterfall” appearance. However, as the injury effect becomes maximum, the final segment of T develops a sharp upward volt-


a
b
t

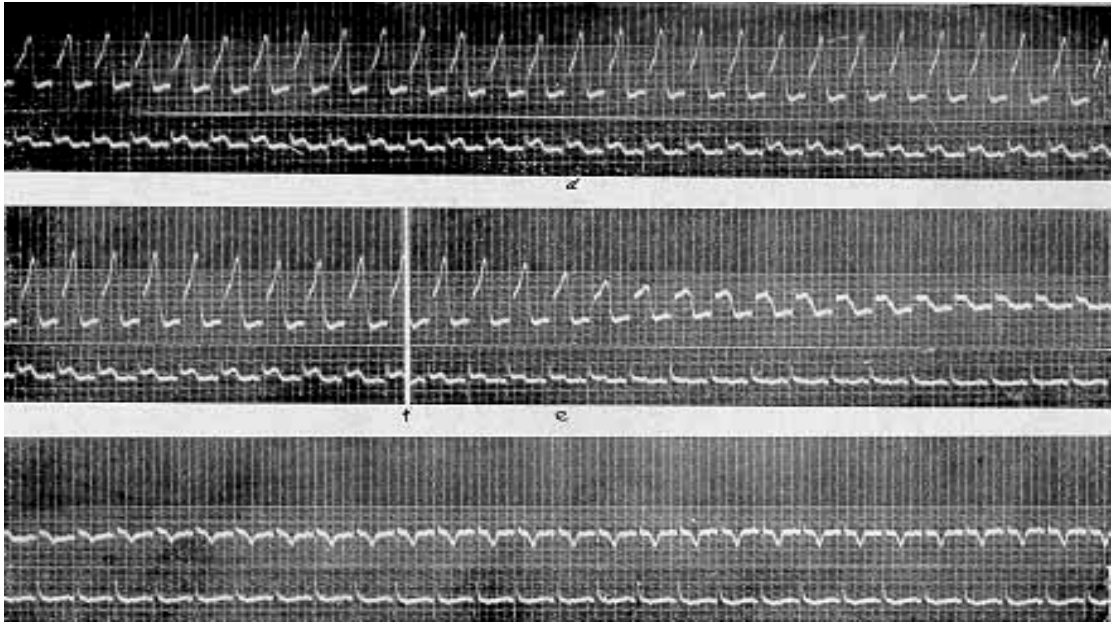


Fig. 3 - The negative-T pattern. A continuous strip recorded before, during, and after a temporary experimental occlusion in dog of ninety seconds duration. The bottom curve of each row is Lead I. The top curve is a unipolar direct lead taken with the exploring electrode superjacent to the region ordinarily irrigated by the occluded artery. Occlusion began at the white time signal indicated by the arrow, a and b show the ischemia phase. c is the transition phase. d is the injury phase. Occlusion ends at the signal in strip e, after which e and f show a return to the control form. (See Figs. 6 and 7 of Reference 15).

age peak which ultimately disappears in about ten minutes if the occlusion is continued. We have referred to this transient phenomenon as the potassium effect of injury since it is known that the element is released from injured cells and since its action on excitable tissue can produce the required changes. [17]

When the occlusion is terminated arbitrarily the evolution of the pattern is interrupted at once and the pattern returns to its control form in a time period which is roughly proportional to the duration of the occlusion. Thus, the pattern of an occlusion of ninety seconds returns to its control form in ten seconds, whereas the pattern of an occlusion of forty or fifty minutes requires twenty-five or thirty minutes for return to its control form. In the more prolonged occlusions the injury phase of the pattern tends to continue without change after the potassium effect disappears. In some experiments the upstroke of R, which constitutes the initial QRS movement and which heralds the approach toward the exploring electrode of the accession wave in the subjacent ventricular wal, [7] was observed to break down gradually into the formation of a Q as early as eleven minutes after the onset of occlusion. In other experiments, the QRS break-down occurred within twenty or thirty minutes after the onset of occlusion, or not at all, even though the occlusion was continued for forty odd minutes.

Blumgart et al. have shown that the duration of occlusion in dog must be about twenty minutes or more if myocardial necrosis is to occur. [18] However, the duration of the injury effect after occlusion ends is proportional to the duration of occlusion whether or not the latter is sufficiently prolonged to lead to myocardial necrosis. We believe that these observations permit one to ascribe the irreversible QRS changes to the potential of the necrotic muscle (which conducts but does not generate electricity), and the ischemia-injury effects to the physiologically disturbed but pathologically normal muscle which lies in the immediate neighborhood of the necrotic muscle. More-over, if no myocardial necrosis occurs, as is the case for occlusions of fifteen minutes or less, the ischemia-injury pattern displays temporary changes in the final ventricular deflections of a kind which are altogether similar to those which occur in connection with myocardial infarction. Consequently, the ischemia-injury effects are not necessarily diagnostic of myocardial infarction. Their temporary character is in contrast to the permanent QRS changes which are diagnostic [7] of myocardial infarction.

The ischemia phase of the ischemia-injury pattern would be of academic interest only if it were invariably traversed in a brief period of thirty seconds; however, this is emphatically not the case. Experiments with subtotal occlusion show that the ischemia phase may be prolonged according to the duration of subtotal occlusion. Moreover,

the amplitude of the inverted T, other factors being equal, may be increased according as the occlusion is increased and the pattern be made to evolve into and out of the injury phase according as the partial occlusion is increased or decreased. High grade occlusion is ordinarily required in order to obtain the injury phase.

Experimental occlusions of fifty minutes or less produce no prolonged electrocardiographic changes. All of the so-called prolonged changes which appear on or after the first postoperative day are ascribed by us to a traumatic postoperative pericarditis. Direct leads from the ventricular surface show conclusively that regions of muscle irrigated by the previously occluded artery are not responsible for generating the so-called prolonged electrocardiographic changes. [16] Previously, these changes had been ascribed to temporary occlusion. [18,19,20]

Several noteworthy disturbances of cardiac mechanism have occurred during experiments which deal with temporary occlusion. Commencing with the onset of the occlusion period, there occurs a danger period of several minutes during which multiple ventricular extra-systoles, paroxysmal ventricular tachycardia, or ventricular fibrillation may occur. With the more prolonged temporary occlusions a second danger period occurs immediately upon sudden termination of the occlusion. Ventricular fibrillation is not uncommon. In one instance, paroxysmal ventricular tachycardia commenced at once, was immediately terminated by reestablishing the occlusion, and continued to recur intermittently with temporary release of the occlusion for fifteen or twenty minutes. Finally, a gradual reopening of the artery permitted a normal mechanism to continue. We did not ascertain if ventricular fibrillation was less likely to occur when the occlusion was terminated gradually as compared with suddenly. Obviously, a solution of these matters might prove of some practical value.

In a minority of our experiments the preparatory procedures for actual coronary occlusion were attended by a striking sinus tachycardia. The associated occlusion patterns were atypical in that the ischemia phase was ill defined or skipped and an injury type of pattern developed rapidly. The tachycardia may have affected a change in the dynamics of coronary flow. In some instances the tachycardia developed shortly after induction of anesthesia (Nembutal). In other instances, the tachycardia developed upon opening the thoracic cage.

CLINICAL CONSIDERATIONS

The ischemia-injury effects are of two clinical varieties, acute and chronic. The former is apt to appear in curves recorded from subjects who give a history of cardiac pain, whereas the latter variety is frequently observed in curves recorded from subjects who complain

of attacks of paroxysmal dyspnea. The attacks of dyspnea usually have hypertension or syphilis as their etiological basis.

The acute form is probably observed most frequently in connection with acute myocardial infarction. It probably occurs most frequently, however, in connection with the more benign attacks of heart pain which are frequently referred to by the vague term "angina pectoris". Here, the injury effect is not likely to be observed unless the curve is recorded during the occurrence of the pain. In a majority of these cases the injury effect is evidenced by a downward displacement of the RS-T junction in Leads I and 11, with little or no displacement in Lead III. The precordial leads at points superjacent to the left ventricle display a downward displacement (often striking) of the RS-T junction (Fig. 4a). Although many such curves have been published, the authors have seen no example which has included the esophageal leads. Let us first suppose that the electrocardiographic picture is that of injury-with-the-rule (see p. 5). The axis of injury points in the direction of the valve openings where no ventricular muscle exists. In order to escape this dilemma it has been proposed that the axis of injury is directed dorsally as well, which indicates that the injury is posterobasal. [21] If this were actually the case, esophageal leads recorded with the exploring electrode superjacent to the injured region would display upward displacements of the RS-T junction. Let us next suppose that the specified electrocardiographic picture is that of injury-against-the-rule (see p. 6). The axis of injury points toward the center of the left ventricle from a centroid which is located near the ventricular apex (Fig. 4a). Consequently, a generalized subendo-cardial injury is hypothesized in order to account for the specified position of the centroid. This situation is the approximate geometrical inverse of the injury distribution encountered in certain cases of pericarditis. We have been unable to devise a satisfactory method for producing experimentally a diffuse subendocardial injury. Others have made what we regard as unsatisfactory attempts. [22] Certain clinical observations which are to be reported elsewhere have led the senior author to believe that the latter distribution offers the correct interpretation of the specified electrocardiographic picture. We predict, therefore, that when appropriate esophageal leads are recorded from a subject whose curve meets the other requirements, they will display downward, rather than upward, RS-T junction displacements.

It is difficult to suggest more than two immediate causes for the diffuse subendocardial injury. The attacks of pain are usually brief and tend to recur for a period of years in subjects who ultimately die, more often than not, of myocardial infarction. When death occurs early in the course of the attacks, it is sudden and comes during or at the end of an attack and is, no doubt, related to the onset of ven-

tricular fibrillation. The coronary arteries frequently, though not always, show degenerative changes. The myocardium shows no evidence of recent infarction. Hypertension is present in about fifty percent of these patients. The pain has received careful clinical study on occasions too numerous to mention. Of particular interest is the more recent observation that, of subjects who complain of pain on exposure to cold, many can induce the pain by holding a cube of ice in the hand .[23] Here, the metabolic requirement and the heart work is not increased as in the case of exertion, emotion, or eating.

Nitroglycerin, an antispasmotic, characteristically relieves the pain after which the electrocardiographic changes more gradually revert to their control form. The electrocardiographic changes may be induced frequently when the pain fails to occur, or, an attack of pain may be unattended by detectable electrocardiographic changes. The evidence, so it seems to us, strongly suggests that the prime physiological event which accounts directly for the pain and usually for the ischemia is a generalized coronary spasm with diffuse subtotal occlusion of the coronary arteries. If the arteries are rigid with degenerative changes, the occlusion and its dependent factor of myocardial ischemia may be minimal with minimal or no electrocardiographic changes even though the spasm and pain are severe. If fixed degenerative changes have limited the reserve for increased coronary flow, an increased demand for heart work may cause ischemia with its electrocardiographic evidence in the total absence of cardiac pain. If a sharp-edged athero-clerotic plaque is present which gives rise to a semirigid arterial wall, spasm may force the edges of the plaque into the vascular subintimal tissues with resulting hemorrhage and coronary thrombosis. The severe attacks of heart pain which ordinarily attend myocardial infarction (with or without an associated coronary thrombosis) suggest a severe local coronary spasm and contrast to in sharp contrast to the relatively benign pain of generalized coronary spasm. It is highly probable that coronary thrombosis may result from purely degenerative changes in the vessel walls which do not involve the physiological element of local coronary spasm. Such an event would, according to our present view, lead to a painless myocardial infarction provided, of course, that the rate of occlusion is sufficiently rapid. For obvious reasons this event must he much more common than a review of the reported cases might lead one to believe. It is this group of cases which deals a fatal blow to the prevalent idea that cardiac pain arises from myocardial ischemia. Certain authors have repeatedly emphasized the dissociation of the electrocardiographic evidence of myocardial ischemia and the occurrence clinically of heart pain .[24,25,10]

The problem of accounting for injury-with-the-rule as the result of local coronary spasm and injury-against-the-rule as the result of general coronary spasm does not seem to offer insurmountable dif-

ficulties. In the case of the latter, the possibilities for collateral circulation, other than from the ventricular chambers, is greatly limited; whereas, in the former, the arterial plexus of Gross [26] which is situated within the subendocardial muscle is, no doubt, important in maintaining the integrity of the subendocardial lamina of the injured region, a situation which is fundamental for the occurrence of local injury-with-the-rule. [10]

The electrocardiographic pattern of diffuse subendocardial injury-against-the-rule may be obtained with minimal, but nevertheless characteristic, changes from certain subjects who are given exertion tests of various kinds, [27] or low oxygen inhalations. [21] Heart pain may or may not occur. The prognostic significance of these changes is necessarily unreliable, but their occurrence permits a diagnosis of transitory local ventricular ischemia (injury). A diagnosis which implies pathologic or physiologic coronary artery changes is not justified unless the whole clinical picture is unequivocal. Ashman and Hull [21] and Grabiel and White [29] have published typical patterns of the kind under discussion which were recorded from young subjects with a fatal diphtheritic myocarditis. Isolated myocarditis may be confined to the endocardial laminae of the left ventricle and may, therefore, produce the specified electrocardiographic picture. With myocarditis, the breakdown of the QRS complex, particularly in the precordial leads, is of grave significance.

A distinctly different electrocardiographic pattern is that produced when a subdivision of the coronary arterial tree is involved by spasm. The associated injury is with-the-rule, and the exploring electrode, when placed superjacent to the injured region, records a pattern characterized by upward displacements of the RS-T junction. The inverse direction of displacement occurs if the electrode is across the heart from the injured region. [5] The sense of the RS-T shift in the limb leads may be used to reckon the direction of the axis of injury which points from the center of the left ventricle toward the center or centroid of the injured region. The RS-T junction displacement is positive in Lead I and negative in Lead III with anterolateral, and negative in Lead I and positive in Lead III with inferoseptal, involvement (Fig. 4b). With anteroseptal and with strictly posterior involvement, the limb leads tend to show no RS-T junction displacements. Moreover, the attacks may be mild so that only primary T-wave changes may occur. The direction of the sharp voltage peak of T is the inverse of that described for the RS-T junction in connection with injury-with-the-rule. The comparative long duration of the T-wave changes enhances their diagnostic value. However, their transient occurrence in approximate association with suspected heart pain has exceptional diagnostic value. If the attacks of pain are frequent and the electro-

cardiographic changes characteristic, the diagnosis of impending infarction may be entertained. [10,2]

The presence of an acute local ventricular ischemia or its electrocardiographic equivalent is by no means evidence of disease which involves the coronary arteries primarily, or of an acute myocarditis.

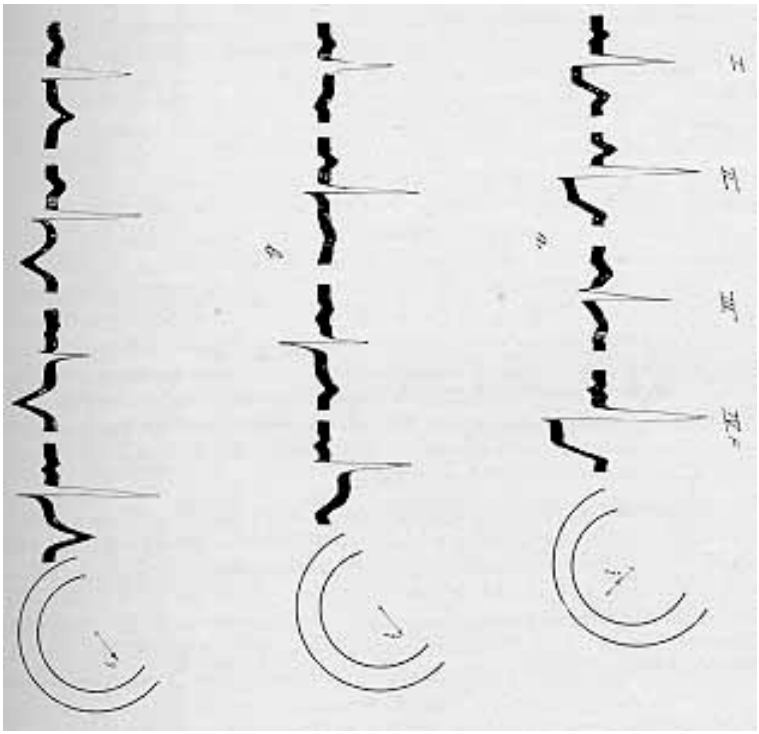


Fig. 4 - (a) Injury-against-the-rule. The injured region is diffusely distributed about the endocardial surface of the left ventricule. The right hand diagram indicates the direction of the axis of injury i drawn from the centroid of the injured region toward the center of the left ventricle.

(b) Injury-with-the-rule. The injured region is in the lateral free wall of the left ventricle. The right hand diagram indicates the direction of the axis of injury i drawn from the center of the left ventricle toward the center of the injured region.

(c) Acute local ventricular ischemia of the region ordinarily irrigated by the right coronary artery. The right hand diagram indicates the direction of the ventricular gradient pointing away from the ischemic region. See text.

A dissecting aneurysm may compress one or both of the coronary ostia, [10] the Herxheimer reaction of syphilitic aortitis may rapidly close a coronary ostium, generalized arteritis may involve the coronary arteries incidentally, and neoplasm may invade the heart wall and its arteries.

The diagnosis of the chronic variety of local ventricular ischemia requires the electrocardiographic evidence of characteristic primary T-wave changes similar in kind to those described as evidence of acute local ventricular ischemia. The appearance of the T-wave changes is a matter of months or years rather than seconds or days, and the disappearance is usually interceded by death. Analysis of these curves with the ventricular gradient discloses that the muscle units responsible for the changes are those at the ventricular surfaces of one of two general regions, that ordinarily irrigated by the left, and that ordinarily irrigated by the right, coronary artery. When syphilitic aortitis constricts one of the coronary ostia, the electrocardiographic changes are usually in agreement with expectations. With essential hypertension a local distribution of the kind indicated is not easily accounted for. Moreover, a subacute evolution of characteristic T-wave changes occurs rather frequently during the course of acute glomerular nephritis. The first mentioned region is the more frequently involved. A satisfactory explanation cannot be offered but it is safe to state that the involved region acts electrically the same as it would if it were supporting a chronic local ischemia.

Anterolateral involvement is evidenced by a sharp voltage peak which is negative in Lead I and in precordial Leads V_5 and V_6, and positive in Lead III. Inferoseptal ischemia produces T changes of a similar kind but in the inverse direction (Fig. 4c). A superposition of the common variety of primary T changes and the secondary T-wave changes of left ventricular preponderance produces an electrocardiographic picture which has received the vague mechanical term “left ventricular strain”. The superposition of primary T changes which denote local ischemia in other locations upon similar secondary T changes yields different patterns of equally distinctive form which belong fundamentally to the same category, but which have received no specific mechanical terms. The difficulty is avoided by using terminology which directly relates the electrocardiographic changes with the myocardial changes upon which they depend.

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