The Heart Muscle and the Electrocardiogram in Coronary Disease

III. A New Classification of Ventricular Myocardial Damage Derived from the Clinicopathologic Findings in 100 Patients (Part Two)

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NOTE: In view of the length of this article, it is being published in two issues. This issue contains the Discussion and References. The September 1955 issue included the Introduction, Methods and Results. The synopsis of the article is repeated below.—ED.

Methods, designed to study in detail the lesions resulting from coronary disease and to reconstruct accurately the form of all ventricular muscle lesions, have been applied to 100 consecutive electrocardiographed patients who were found to have at least one severe coronary narrowing. Reclassification of lesions into four categories was found necessary to deal with the patterns of damage disclosed. This approach permits conclusions regarding evolution of muscle damage, relationships of arterial obstruction to muscle damage distribution, and the significance of ischemia which would have been impossible otherwise. The value of the new classification for electrocardiography will be discussed in a subsequent section of the report.

DISCUSSION

1. Representative Character and Peculiarities of the Statistical Sample

We believe the most important feature of this study to be the demonstration that patients with obstructive coronary disease may have a number of basically different myocardial damage situations, which can be defined simply and unambiguously under four categories. All our patients with muscle damage could be assigned to one or another of these with little difficulty. The exact percentage composition of our sample is of course of little importance, since it might vary considerably for another hundred cases. It is noteworthy, however, that all four basic situations proved to be common and therefore demanding of clinical and investigative consideration.

Certain deficiencies in the size and composition of our sample should be kept in mind. A major distributional distortion must have been introduced by the requirement that all the patients be electrocardiographed. Undoubtedly an unselected necropsy series of patients over the age of 40 years would have yielded a larger percentage of scars, especially the small regional types that were not major causes of death. Indeed, our preliminary report1 included 35 such scars, more than half of which were discarded from the present sample because they lacked electrocardiographic documentation. Study of a series of patients with typical uncomplicated anginal syndromes who died of some "noncoronary" cause would be of great interest. Only a few of our patients (all in group I) are in this category. Certain widespread damage situations are not well enough represented, notably, hearts with small, regional scars plus acute, subendocardial infarction confined to another region; for they must represent a common transitional state.

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This investigation has been supported since September 1949, by a grant (USPH 398) from the National Heart Institute, National Institutes of Health, Public Health Service and previously, in part, by the Life Insurance Fund for Medical Research (Sayen 1947–8).
between group I and group III presumably not as often lethal as other states. Two large (transmural) lesions in the same heart, each with a regional distribution, were found in only two instances. However, in view of the fact that at necropsy 10 per cent of the hearts contained a large regional scar and none had acute damage in any other region, we thought that more than one large (transmural) lesion in the same heart was an actually uncommon situation rather than a failure of our sample to be representative.

We would not expect the various myocardial situations here described to have similar frequencies if based on series of routine autopsy protocols, however painstaking or voluminous. Common errors in routine necropsies are failure to find more than one portion of the widespread or multiple scars of group III patients; missing altogether the widespread acute lesions of group IV patients or, having found only part of the necrosis, describing it as localized damage; and failure to discern the small subendocardial posterior, posterolateral and lateral scars that in our experience were the earliest and commonest of healed lesions. Such errors would automatically lead to exaggeration of the size of group II with its “anterior” and “posterior” massive lesions, which are almost never missed and seldom misinterpreted; to shrinkage of group I with its small subendocardial “posterior” and “lateral” single lesions (especially likely because as a rule these patients died of something besides coronary disease); and to replacement of groups III and IV by dismissive mention of “diffuse” scarring or “multiple lesions” considered to be of a complexity too extreme to repay meticulous study.

An unexpected and important finding was the peculiarly high or low incidence of certain types and combinations of muscle damage, in contrast to the rather even distribution of stenotic and occlusive coronary lesions. These phenomena were characteristic of the sample as a whole and not a consequence of our method of grouping the cases. However, the classification derived from our data brought out certain of these peculiarities of muscle lesion distribution very strikingly.

We have noted that small regional lesions were much commoner in the right and the left circumflex coronary regions than in the anterior descending region, whereas “anterior” were by far the commonest type of large regional lesion. In the whole sample, however, anterior damage was no less common than damage in other locations. From this, it followed that “small” anterior lesions strongly tended to be associated with earlier or coeval damage in at least one other region. Perhaps the simplest general summation of these phenomena is to say that damage in the left ventricle (except for the single massive, regional infarcts) tends to begin elsewhere than in the anterior coronary region. In almost four-fifths of the 74 scarred hearts, the earliest scarring was in the right or left circumflex regions: that is, the posterior wall, the basal two-thirds of the lateral wall, and a small part of the posterior septum. Since the incidence of old coronary obstructions was essentially similar for all three regional arteries, other causes must be sought for the above findings.

Differences in the exact severity of obstructive lesions and in their proximity to the origins of the major arteries must have been of great importance. Our method of analyzing the data does not take these into account. We have, further, no way of estimating differences in the speed of development of old coronary obstruction (narrowing or occlusion) although this must be of crucial importance for the development of collateral circulation. Moreover, we could not evaluate the effects on the collateral circulation to any myocardial region of obstruction in the vessels from which the collateral circulation itself must have been coming. It should be borne in mind, however, that stenosing or occlusive coronary lesions might have differed significantly in their myocardial effects not only for the various reasons just mentioned, but because of differences in physiological pressure and flow relationships in the regional muscle perfused by each of the three major arterial trunks. In this connection certain peculiarities of the right coronary region in man are worth considering.

The long right coronary artery’s course is mainly over the right ventricle, in the muscle
of which, and in that of the right atrium, all but its most distal branches ramify (see fig. 1). These distal branches supply the posterodiaphragmatic left ventricle in at least 80 per cent of human hearts. Blood flow in the left ventricle’s walls during systole must be slight. On the other hand, mural right ventricular pressures are normally low enough to permit continuous perfusion of the muscle even during systole. With a normal right coronary arterial lumen, the pressure drop due to right ventricular systolic perfusion may not seriously prejudice the left ventricular muscle at the distal end of the artery. But any right coronary narrowing by atheroma should put the distal left ventricular muscle at a great disadvantage as compared with the right. Furthermore we have seen two hearts (not in the statistical sample, of course) with posterolateral scars and no coronary narrowings at all.

Collateral blood supply to left ventricular muscle in the distribution of the distal ramifications of the left circumflex coronary artery must come in large part from the right coronary artery. Therefore this muscle also (fig. 1e, areas 15 and 23) might have a more precarious blood supply in the presence of even slight right coronary and left circumflex obstruction than would muscle elsewhere in the heart. Unfortunately there are so few instances of monkeys, dogs and other animals having the common human type of long right coronary artery that experimental testing of such hypotheses is difficult.

While small circumflex regional lesions were relatively common, large circumflex regional lesions were not. This fact suggests that the circumflex region can become well supplied with collateral circulation from at least one neighboring region. The circumflex’s smaller size may be the entire explanation for this. That the left circumflex artery has no right ventricular distribution may perhaps be another favorable feature. A small amount of left atrial perfusion during systole must of course occur. In any case it appeared that massive circumflex regional damage not only required severe obstruction of both the other major arteries but always involved damage in one or both of these distributions previous to, or at the same time as, that of the circumflex artery.

Finally, to give brief attention to the effects of combined regional ischemia: right-plus-circumflex and anterior-plus-circumflex region combinations together comprised less than 20 per cent of the total for both widespread damage groups. In contrast, either right-plus-anterior combinations or damage in all three regions were found about equally often in four out of every five widespread damage patients. From these phenomena it appears that severe interference with perfusion of both arteries supplying the interventricular grooves is especially likely to be found in hearts with widespread scar or infarction, at least at autopsy.

These arteries constitute the main blood supply to the septum, or intracardiac portion of the left ventricle. An important feature of the normal septum is its profuse intramyocardial vasculature supplied by many penetrating branches from the undersurface of both the “descending” arteries. The septal vascular bed seems to be strategically placed for shunting blood between the anterior and the right (posterior) coronary regions and may constitute an important source of myocardial circulatory flexibility. Once both the main sources of septal circulation are throttled, to the point where at least some muscle is lost in both the anterior and right coronary arterial regions, the patient joins (by definition) one of the “widespread damage” groups. However, the surprising predominance of situations of this type at necropsy—four-fifths of all “widespread damage” hearts—suggests it may be more often lethal than are other combinations.

2. The Necessity of a New Classification

Our lines of inquiry concerning muscle infarction, scar and localized ischemia seem to neglect other questions which perhaps arise even more commonly in the minds of physicians confronted with “coronary” patients. Has there been a recent coronary thrombosis?, is there any old coronary occlusion? and is there reversible coronary insufficiency or spasm? These questions, framed in terms of the
coronary arteries, parallel the lines of inquiry we listed previously. Answers to the questions regarding recent thrombosis and old obstructions have been provided in our data charts. The third question cannot profitably be answered in the present state of our knowledge, since the very existence of coronary spasm is still debated and, in man at least, "coronary insufficiency" is another word for myocardial ischemia. (See part 3 of this Discussion.) We gradually came to realize that descriptive terms derived from coronary lesions or circulatory disturbances were much less valuable for ordering our data or our thinking than we had supposed they would be at the outset of this investigation.

Unlike the situations in experimental animals (see Ischemia), we could not regularly define human heart muscle damage at necropsy in terms of the coronary lesion that must have caused it. The pathologic hallmark of coronary artery disease in man is segmental, epicardial coronary narrowing. For this there is no time scale and, unless damage is found, no way of estimating circulatory disturbance in the muscle supplied. Thus, in our sample, even in the exceptional cases wherein only one artery was narrowed, we were unable to say how long severe stenosis had been present. If at necropsy acute thrombosis of an insignificantly narrowed vessel had proved common, we might have thought it roughly analogous to arterial ligation in the dog, but such situations proved comparatively rare.

Thus, in reference to a myocardial lesion in man, we could not say, what has happened is the usual consequence of blocking this size artery, for we did not know whether the artery had been of normal size before it was blocked, or how rapidly any total obstruction had become complete. Indeed, except for coronary embolism or the rare instance, where the surgeon had to ligate a coronary branch in a patient thought to have a normal coronary circulation, it seemed unlikely that we ever could tell what the "expected" muscle sequelae of sudden occlusion of any one coronary vessel in man might be. There seems little hope of distinguishing, by their coronary lesions alone, patients with two or more severely stenosed major arteries; a situation the assessment of which was extremely difficult even in suitably prepared experimental animals.

The coronary lesions thus had a peculiar status in our study. They were essential for evaluating particular muscle lesions, but, once the details of any given ventricular myocardial situation had been established, the coronary lesions became not only inessential but sometimes sources of confusion, in part no doubt, because our methods for estimating collateral circulation were inadequate.

For our purposes, the most important things about the coronary tree in human atherosclerosis were (1) the originally triradial character of the circulation, and (2) the high frequency of stenosing lesions in the larger epicardial trunks, resulting (3) in restrictions of flow (or flow capacity), which almost always differed in degree of severity for one or all three coronary regions. Once the potentially ischemic regions (those at least with a significant coronary narrowing) had been grossly identified at necropsy, muscle lesion evaluation provided the only definitive judgment of actual flow impairment. During life, of course, no direct evidence as to the state of the coronary arteries can be elicited. For purposes of classification and consideration in the clinic and at necropsy, therefore, we felt that arterial lesions could not be given first place.

Our attempts to describe myocardial situations by conventional nomenclature were frustrated by (1) its reliance on anatomic, localizing terms and (2) its inability to deal efficiently with hearts containing multiple lesions. Not more than a third of our hearts contained single, typical "anterior," "posterior" or "lateral" infarcts. They, and the few hearts with more than one lesion but with each infarct or scar having a fairly typical shape, could possibly be described well enough by redefining terms in a prolix fashion; but even this was impossible for the remainder, which comprised over half our sample. For them the ordinary coronary "architecture", on which conventional nomenclature depends, no longer had much meaning. The original coronary distribution patterns seemed to have been
blurred, or erased altogether so far as the shape of the muscle lesions was concerned (see below). Since it was impossible to describe even the anatomic location and distribution of myocardial damage by means of the usual terms, it was hopeless to classify groups of hearts on such a basis. The usual "general" criteria of classification for muscle lesions, "large" or "small," "multiple" or "diffuse," "recent" or "old," failed to bring out important and useful distinctions; indeed, this tended to keep us from paying proper attention to such distinctions. Forced into formulating a new vocabulary, our best approach proved to be classification on the basis of size for hearts with single, regional lesions and of age for those with multiple or widespread lesions. This avoids the initial attempt to describe specific anatomic location.

Of course no classification for coronary disease can dispense with description of anatomic location, but such data were preserved with accuracy in our maps. The frequency charts based on our classification also display certain pertinent pathologic structural relationships in groups of hearts that would not otherwise have been apparent. In the case of particular anatomic damage patterns that were common and consistent enough, verbal reference could easily be achieved by new names.

As in the case of anatomic location our proposed classification permits, but does not directly depend upon, study of the coronary arterial lesions. Indeed it must be remembered that to classify any heart accurately, the ventricular myocardial lesions must first be mapped, a procedure into which the results of both anatomic location and coronary lesion study must always enter.2, 3

3. Ischemia

While our anatomic data have necessarily been confined to only two of three aspects under which the heart muscle in coronary disease must be considered, namely, scars and recent damage, the anatomic backgrounds cannot be properly interpreted without consideration of a third major aspect of the natural history of coronary disease, the threshold and the configuration of localized ischemic areas.

For this discussion we define "ischemia" as a deficiency of myocardial blood supply severe enough to produce evidence of disturbed function: preferably measurable by objective tests but in man also reflected by the anginal syndrome. Thus we can describe myocardial ischemia clinically only as a reversible state reflected by anginal pain or certain electrocardiographic abnormalities, the latter sometimes present only in association with anginal pain or elicited by stress (most often increases of cardiac work or controlled anoxia). The severity and duration of stresses required to elicit evidences of ischemia are rough measurements of its threshold. The criterion of reversibility is necessary because irreversible ischemic states, immediately preceding frank infarction, seem still to be inaccessible to study or in vivo definition.

In experimental animals we can define and measure localized ischemia with some precision. Upon the establishment of a sufficiently severe segmental coronary narrowing, there ensues a fall in local oxygen tension, disturbed local repolarization, increased muscle irritability, and diminished strength of muscle contraction.15 These signs of localized ischemia follow narrowing of lesser severity if accompanied by reduced coronary perfusion pressure,21 increased blood viscosity, anoxic stresses,17 or other disturbances of the general coronary circulation sufficient to put muscle with restricted blood flow at a disadvantage. Localized myocardial ischemia is then a consequence of either diminished local blood flow or inability to respond to a call for hyperemia in a part (or parts) of the ventricular muscle when the remainder has a normal or relatively normal blood supply.

It is important to differentiate localized ischemia, with its low threshold situations and easily-upset balances, from what might be called diffuse or "physiologic" ischemia. Extremely severe dynamic or anoxic stresses may damage the heart muscle even in the absence of stenosing arterial disease. In animals subjected to violent exertion (especially when anemic), acute necrosis has been demonstrated
in the left ventricle and septum. It has been described in certain patients with pulmonary embolism and carbon monoxide poisoning, although in most instances coronary disease had either been demonstrated or had not been excluded with certainty. These situations, however, are characterized by high thresholds. It is quite difficult to produce myocardial necrosis this way in animals with “normal” coronary arteries. Anatomic changes are uncommon, difficult to interpret, and very limited in extent when they do occur: at most, a few scattered foci of necrosis in trabeculae near the left ventricular cavity.

No myocardial changes precipitated by defective blood supply can be truly “diffuse.” It is well known that the inner layers of the systemic ventricle—the left ventricular walls and their intracardiac continuation in the septum—constitute a myocardial point of least resistance. Differences in intramural pressure and a remoteness from their blood sources must cause these inner layers of the systemic ventricle to be at a disadvantage, not great perhaps but ineluctable if sufficient stress be applied. At present such a disadvantage is difficult to demonstrate and almost impossible to measure. The ordinary experimental or clinical ischemia indices, so far as we know, depend on there being considerable amounts of relatively “normal” left ventricular muscle, which can keep a circulation going and permit a less advantageously supplied portion of the heart to be forced into mechanical failure by the intraventricular pressures generated by the “normal” muscle. Only under these conditions can the disturbances in muscle contraction and repolarization which we must depend on for early experimental recognition of ischemia be expected to develop.

In man, well-documented cases of muscle necrosis without coronary stenosis are rare, except when aortic valve disease is present. Aortic stenosis and insufficiency provide transitional situations that may produce medium or low threshold ischemia with relative evenness of coronary flow deficiency throughout the ventricles. While in living patients with aortic valve lesions it is frequently impossible to exclude inequalities of coronary lumen patency due to ostial (syphilitic) obstruction or segmental atheroma, an appreciable number of patients with aortic valvular disease and clearcut histories of anginal type pain come to necropsy with entirely patent coronary vessels and yet with recent subendocardial left ventricular necrosis.

Thus there is need for terminological distinction among at least three ischemic situations: (1) diffuse “physiologic,” high-threshold ischemia; (2) diffuse “aortic,” medium-threshold ischemia; and (3) the “localized,” subventricular, low-threshold ischemias that are limited almost completely to coronary disease. Such distinction has been made difficult because it is now customary to refer indiscriminately to any of the localized or generalized, low- or high-threshold types of ischemia as “coronary insufficiency,” thus emptying the term of useful significance. If it is to retain any clear-cut meaning at all, “coronary insufficiency” should be reserved for the “aortic” type of generalized ischemia, or experimental analogues of it. As it is now, the term is actually an obstacle to critical consideration of myocardial ischemic situations.

Indeed, it is not enough to designate three types of myocardial ischemia. Our studies suggest that at least two varieties of localized ischemia must be borne in mind, regional ischemia and widespread ischemia. The latter is a type of localized circulatory inadequacy affecting more than one coronary region. It resembles the “physiologic” and “aortic” varieties of generalized ischemia in damaging especially the subendocardial layers of the left ventricle and septum, but differs from “physiologic” ischemia in having a low threshold. It is a step beyond regional ischemia into a still more severe distortion of the coronary perfusion “architecture.”

In our sample of human coronary disease, it was not uncommon to find widespread acute infarction affecting parts of the distributions of two major regional arteries, even in the absence of acute coronary thrombosis. In 40 per cent of the “widespread acute infarction”
hearts (group IV), no recent coronary thrombus was demonstrated. Furthermore, single acute thrombi were sometimes associated with infarcts which, while they involved only a portion of the original distribution of the affected artery, at the same time, extended well beyond that region.

Such phenomena may signify advanced distortion of the original coronary perfusion "architecture." Progressive coronary obstruction presumably had caused collateral circulation to become one of the major factors conditioning the pattern of perfusion, not merely in one region, but throughout most of the ventricular muscle. While epicardial vessels doubtless contribute something, it is clear from injection studies of hearts, and consideration of the rather strict limitation of atheroma to epicardial arterial trunks, that intramyocardial vessels must be the chief conduits of collateral blood flow. Such flow can be expected to blur or change completely all the original patterns of epicardial arterial distribution.

The response to stress of a heart containing a low-threshold widespread ischemic area might be expected to differ considerably from that of a heart whose low-threshold muscle is restricted to not more than a single coronary region. The difference would not have to be a simple quantitative one, proportioned to greater restriction of total coronary blood flow. Any failure of muscle contraction consequent to ischemia of crucial severity would, in a regionally ischemic heart, consist of a localized systolic "bulge" such as can readily be reproduced in the experimental animal. In a widespread ischemic heart the mechanics of systole would be deranged in a much more complex way because of failure of muscle contraction, especially of the inner layers, throughout most of the left ventricle. With prolonged regional ischemia, the common consequence is infarction and ultimate scar formation (predominantly subendocardial). With widespread ischemia, the consequences are almost unknown, though a fatality is not necessarily to be expected. Clearly, however, the more widespread the ischemic zone and the greater the amount of scarring already present in any heart, the less it can "afford to lose" ischemic muscle by frank infarction.

Analogous ischemic situations have been produced in suitably prepared experimental animals. If we obstruct one coronary artery, ischemia is demonstrated regularly in the distribution of this artery but not in those of the others. If the left anterior descending and the circumflex are gradually obstructed without demonstrable ischemia in the distribution of either, and weeks later, a circulatory stress previously harmless to the animal is then added, evidences have been produced of ischemia followed by sudden death or, after a sufficient period of survival, massive acute necrosis in the distribution of both arteries.

In man a simple distinction between widespread and regional ischemia on the basis of coronary lesions alone has not been possible. Multiple severe narrowings were too common, and the efficacy of collateral circulation too difficult, to estimate. However, it seems fair to assume that the occurrence of widespread muscle damage in coronary disease patients provides the soundest basis for inferring the presence of actual or potential widespread ischemia.

Widespread damage was present in more than half our sample, but our data show it must have developed in more ways than one. Many patients suffered recurrent episodes of muscle loss, resulting characteristically in widespread subendocardial scarring. Presumably there must have been residual or potential ischemia at many scar sites. Late (usually terminal) acute infarction episodes under such circumstances often consisted of spotty acute damage near one or more of the old scars, with or without a distinct larger area of infarction. The mass of the recently damaged muscle might or might not have been large but its comparative importance doubtless increased in relation to the amount of ventricular muscle that had already been lost. This general type of behavior was represented by our group III patients. In contrast were the widespread infarction patients of group IV who lost little or no muscle until their potentially ischemic
areas were revealed, wholly or in part, by a terminal infarction.

It was also our opinion that in the same hearts there might well exist localized ischemic zones that differed slightly in their thresholds. One zone might be made ischemic by an exertional circulatory stress or the interference with flow through small vessels that is supposed to follow a fatty meal. A second zone, with a higher threshold, might become involved only when the blood pressure fell severely as a consequence of failure of the first area to contract. Thus a downward spiral of disturbed myocardial function would be initiated. Certainly in some of our widespread infarction hearts, portions of the terminal acute infarct differed somewhat in histologic age. Such phenomena were almost never explainable on the basis of extension of a thrombus or the presence of more than one clot.

The presence of regional or widespread ischemic areas, actual or potential, cannot be left out of consideration either for evaluation of living patients or in clinicopathological retrospect. While we cannot at present quantify ischemia or even make a direct demonstration of its full extent at necropsy, it is possible to make a crude estimate from (1) the original anatomic distribution of the coronary branch or branches most severely or recently obstructed, (2) the degree of distortion of coronary perfusion "architecture" as reflected in the shape of old and new muscle lesions, and (3) clinical data as to threshold and frequency of anginal pain. (Details of our methods of estimation will be given in part V of this study.)

Patients with large and small regional areas of potential ischemia might be expected to differ considerably in their circulatory physiology, both from each other and from patients with widespread ischemic areas. The differences may be further altered by previous myocardial scarring. Indeed, it would seem that the size and threshold of its ischemic area (or areas) might be the most prognostically significant feature of any heart that is the seat of obstructive coronary disease. Whether or not there has been muscle destruction in any area is an important consideration but it is water over the dam, whereas ischemia is pregnant for the future.

4. Answers to the Basic Lines of Inquiry Provided by the Proposed Classification

In summary, we return to the questions that must be asked about any living patient having known or suspected coronary disease.

(1) Is there a low-threshold, localized ischemic area? If so, is its distribution regional or widespread?

(2) How much muscle has been lost and replaced by scar? Does the scar itself have a regional or widespread distribution? In addition to the lowered threshold for ischemia in the immediate vicinity of any scar, is there also an ischemic area involving any considerable part of the residual, anatomically "normal" muscle?

(3) Is there acute infarction? If so, is it regional or widespread and large or small with respect to the viable muscle? Does it involve most of the patient's previously potentially ischemic area or has only part of this become infarcted, so that considerable low threshold muscle is hanging in the balance? How large a scar will the infarct leave if it heals? Can the patient "afford" to lose his low-threshold ischemic areas?

These questions are restated in what might be called the physiologist's order, starting with the initial types of disturbance and with the more fundamental situations. Therefore ischemia must be the central theme. It has to be considered first, and then reconsidered with each of the essentially secondary lines of inquiry regarding old and new damage. Our previous order of questions (in the introductory paragraphs) may be preferable for clinical and pathologic purposes, since it proceeds from phenomena relatively well-diagnosed during life and having important therapeutic indications (acute damage), to those sometimes ascertainable only by the autopsy (scars), to phenomena whose exact status can only be inferred (ischemia). However, regardless of the order, or of the efficiency of the available
means for obtaining the answers, we believe that these three inquiries are of fundamental importance. Questions of this sort must be answered, or at least have attention drawn to them, by any classification for coronary disease that is to have permanent usefulness for clinicians or for investigators.

Answers to the three lines of inquiry, summarized in table 2, are now briefly reviewed.

(1) Is there a localized ischemic area? Our group I patients did not appear to have had ischemia except in the vicinity of their small, localized scars, and thus in a part of, at most, one coronary region; at least, acute necrosis was never demonstrated elsewhere. Thus we conclude tentatively that they had small, regional ischemic areas. Group II patients did not show evidence of ischemia outside the single, large regional lesion or potential area of infarction characteristic of the group. Group III patients commonly presented evidences of having had multiregional or widespread ischemia, its importance presumably being the greater the less was the amount of unscarred
muscle in any heart. They might also have had multiple but successive ischemic areas with or without differences of threshold between potentially ischemic scar sites and muscle not yet anatomically disturbed. These pictures eventually might become very complex. Group IV patients appeared to have had widespread ischemic areas involving the inner layers of anatomically “normal” muscle and jeopardizing much of the myocardium, their configuration being at least revealed, at least in part, by terminal infarction.

(2) How much muscle has been replaced by scar? Only group III patients invariably had ventricular scars, but small regional healed lesions were commonly present in groups I and IV, almost all being subendocardial. Half of group II had a single transmural scar, presumably the residuum of a large localized transmural infarct. Thus the anatomic muscle reserve had been greatly reduced in group III and in some members of group II (that is, in 42 per cent of our series), though in different ways.

(3) Is there acute infarction? If acute infarction was present, group I patients had a “small” lesion that was associated with a low mortality; group II patients had a compact but large through-and-through lesion that very frequently was lethal; group III patients might have almost any type of infarction superimposed on extensive scarring of various degrees; while group IV patients had widespread, subendocardial damage, which in this series was uniformly associated with a fatality. Group IV patients often developed one penetrant area of transmural infarction later in the terminal episode of acute damage. In general their behavior suggested that not all of their potentially ischemic zone was infarcted simultaneously.

Without classification by total ventricular situation the multifarious data of our sample could not have been presented except in the form of a series of individual case reports. We have mentioned certain clinicopathologic features that seem characteristic of patients in each group and that provide ground for thinking the basic situations may some day be better recognized during life. Whether or not our groups have direct clinical relevance, in that they will make it possible to categorize living patients with diagnostic advantage, will be discussed, in connection with electrocardiograms, in part IV. However, their indirect relevance to the understanding of obstructive coronary disease in man seems unquestionable, provided the three lines of inquiry we have defined above are relevant. Indeed, the basic groups, as defined in words or symbolized in schemata, simply epitomize common and distinct combinations of answers to these questions.

If the answers, though differing widely, are yet characteristic for each group, then the groups themselves must be borne in mind whenever the physician looks back upon the course of his patients from the eminence of the necropsy and tries to evaluate methods of clinical study or treatment. Indeed, only after the three proposed lines of inquiry have been followed through, is it possible to make a fair estimate of the most important physiologic feature of any patient’s heart: the strength, size and circulatory reserve of its residual muscle.

One of the many sources of confusion in clinical studies of coronary disease is the difficulty of evaluating ventricular hypertrophy, chamber dilatation and their end results in the form of congestive failure. Coronary disease is the great diagnostic category where “cured” hypertensives abound. In our series we could often document pronounced falls of blood pressure (to normal or much lower figures) which might be transient or permanent. Often, however, we did not know whether high or higher blood pressures preceded any “normal” figures obtained. At necropsy ventricular hypertrophy, best estimated by weighing the muscle, is a fair value only if little or none of it has been replaced by scar. Furthermore, we could not be sure whether muscle appearing under the microscope to be hypertrophic, a difficult and unsatisfactory method at best, had become so in response to a previous systemic hypertension or to the increased work of ventricular emptying. For example, myocardial scarring, with stiffening of the heart walls or a frankly bulging “aneurysm”, must
increase the work of the residual muscle not only by reducing the original number of muscle fibers but also by making mechanical systole laborious and inefficient. In the present study we have not yet evaluated heart weights and data concerning present and previous hypertension. The criteria for definition of our groups are independent of those factors.

Thus, our three lines of inquiry are really preliminary approaches to even more fundamental problems. They are designed to ascertain the background on which localized ischemia, if it has a low enough threshold to be recognized by available methods of clinical study, may occur; and to group together patients with similar anatomic backgrounds and low-threshold localized ischemic areas of the regional as contrasted with the widespread varieties. The first task is the precise definition of groups of patients or animals similar in amounts of available functioning myocardium, in degrees of past or present hypertensive stress, and in mechanical handicaps such as subendocardial scar sheets or transmural scar “aneurysms.” Only then may we hope to study and understand the behavior of the new physiologic world of the “intramyocardial” circulation that collateral, small-caliber vessels have created; and in which the familiar patterns of physiologic behavior or pharmacologic responses may be greatly altered. In such an approach there would seem to be important advantages for the definitive evaluation of therapeutic agents and the clinical or experimental investigation of myocardial dynamics and electrical phenomena in coronary disease.

**SUMMARY AND CONCLUSIONS**

(1) From 250 autopsied cases in which the ventricular myocardium and the coronary vessels were carefully explored, 100 cases were selected on the basis of (1) a severe narrowing of at least one major coronary vessel, and (2) a recent electrocardiogram.

(2) The age, thickness and extent of the myocardial infarcts and scars were plotted for each case on a myocardial map. A record was also made of the presence of recent thrombosis, old narrowing or occlusion in the three main coronary arteries: the left anterior descending, the left circumflex, and the right. In addition, the original anatomical configuration of these three main coronary regions was estimated from the epicardial arterial system.

(3) The myocardial map was subdivided into 24 numbered areas, some of which were shown by means of a review of the coronary artery distribution in all of the cases, to lie almost invariably within the distribution of one and only one of each of the three coronary vessels. These “central” areas were distinguished from peripheral areas in which the coronary artery of supply was either occasionally or usually uncertain (“probable” and “uncertain” areas).

A chart was then constructed with the 24 areas arranged in a simple horizontal row, so that the central and probable areas of each region were kept in groups, separated from each other by contiguous uncertain areas. By the use of appropriate symbols, the character and amount of myocardial damage for each case could be represented along a single line, which made it further possible to demonstrate common relationships in groups of cases.

(4) With respect to the coronary arteries, it was found that in 87 per cent of the cases more than one vessel was severely obstructed. However, in many cases severe narrowing or old occlusion were not accompanied by evidence of scar in the region of distribution. The incidence of old occlusion or narrowing was nearly the same for all three coronary arteries: about 85 per cent. Recent thrombi were found with about one-third the frequency of old lesions, the left circumflex artery being involved less often than the other two.

(5) Concerning the configuration of myocardial damage, it was found that in 42 cases the damage, old or recent, was confined to the distribution area of one coronary artery. This type of damage was called regional, in contrast to the widespread damage found in 56 other cases (two or three coronary regions involved). In two cases there was no damage. The cases of regional damage divided themselves into two approximately equal groups on the basis of the size of the lesion: group I, small regional lesions; and group II, large
regional lesions. The hearts with widespread damage also fell into two groups: group III, widespread scar, 36 cases with healed scar in the central areas of two or more regions; and group IV, widespread acute infarction, 20 cases with this type of lesion in two or more regions, and little or no scar.

(6) This method of classification was simple, and it proved relatively free of ambiguity. It made possible the consideration and rapid comparison of total ventricular myocardial situations for groups of hearts in a way that was not possible with classification by anatomic location or coronary artery lesions.

(7) One important relationship brought out by this method of analysis was the peculiarly high or low incidence of certain types and combinations of muscle damage, despite the rather even distribution of coronary artery obstructions. Isolated small muscle lesions were frequent in the posterior and lateral regions of the left ventricle, but were never found in the anterior region. Large isolated anterior lesions were occasionally seen, but small anterior lesions, though common, were always associated with other, usually older, lesions in other regions of the heart. Muscle damage in the left ventricle tended to begin in regions other than the anterior.

(8) The myocardial lesions appeared to reflect two degrees of disturbance of the coronary perfusion "architecture:" (1) preservation of the usual anatomic arterial distributions even in badly damaged hearts, as in the single, localized lesions of groups I and II, and (2) blurring or distortion of the perfusion patterns because of multiple epicardial artery obstructions and well-developed intramyocardial collateral circulation. This latter type of ventricular situation might develop gradually, as in the multiregional scars of group III, or be revealed suddenly by widespread acute infarction, as in group IV.

(9) Although the postmortem classification was not based on the estimated extent and threshold of localized ischemic areas, scrutiny of coronary lesions and clinical phenomena in relation to muscle damage configurations suggested characteristic and different areas of actual or potential ischemia during life for each of the groups. A clinical classification framework based on localized ischemia was outlined and related to the postmortem groups.

(10) The proposed nomenclature and classification have, we believe, set in order a complex body of data that could not otherwise have been described except as a series of separate case reports. The present report is to serve as an introduction and as an atlas for subsequent papers dealing with the electrocardiographic and pathologic findings.

**Summario in Interlingua**

Esseva elaborate methodos que permitte le studio detaliate dellesiones resultante de morbo coronari e le exacte reconstruction del forma de omne lesiones del musculo ventriculare. Iste methodos esseva applicate a 100 consecutive patientes electrocardiographate qui habeva al minus un sever constriction coronari. Le typos de lesiones observate requireva un reclassification in quatro categorias. Iste procedimento resulta in conclusiones in re le evolution de dannos muscular e le relation inter obstructiones arterial e le distribution del dannos muscular; illo etiam demonstra le significania de ischemia. Previemente isto non essee possibile. Le valor del nove classification pro objectivos electrocardiographic va esser discutite in un section futur de iste reporto.

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The Heart Muscle and the Electrocardiogram in Coronary Disease: III. A New Classification of Ventricular Myocardial Damage Derived from the Clinicopathologic Findings in 100 Patients (Part Two)

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Circulation. 1955;12:530-542
doi: 10.1161/01.CIR.12.4.530
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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