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

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NOTE: In view of the length of this article, it will be published in two issues. This issue will contain the Introduction, Methods and Results, while the Discussion and References will be published in October, 1955.—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.

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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).
THE INVESTIGATION reported in the series of which this is part III was originally aimed at correlating coronary disease patients' electrocardiographic patterns and myocardial damage found at necropsy. We studied some 250 hearts by a serial slice technique that permits systematic gross and microscopic scrutiny of the ventricular myocardium and the major coronary vessels. Our technic and the electrocardiographic and pathologic findings of the first 150 cases were outlined in 1947 in a preliminary report. In it we emphasized the frequency of multiple lesions and the virtual limitation of myocardial damage to the left ventricular walls and the septum, especially the layers near the left ventricular cavity. We also called attention to the efficiency of electrocardiography in diagnosis and localization of massive damage in the anterior wall, apex and posteroseptal regions of the left ventricle, as well as other anterior lesions that produced breaks in the precordial lead pattern. The limitations of electrocardiography with respect to other areas were noted as was its frequent failure, even when performing most brilliantly, to reflect more than a fraction of the damage actually present.

Part I of our series dealt with the general problem of collecting data for clinicopathologic studies of coronary disease. We discussed some of the inconsistencies and confusion in the literature which have resulted from the mistakes to which autopsy studies, not aimed primarily at study of the ventricular muscle, are liable such as the complete overlooking of some lesions, misinterpretations of their age so that acute damage and healed scar were confused and incorrect determination of their positions and anatomic relationships. We also pointed out that these common errors were not random but occurred because some types or positions of damage are much harder to recognize than others, with the serious consequence that the size of a clinicopathologic series was by no means necessarily a protection against progressive distortion of data.

To secure more complete, reliable data we modified methods in general use as follows: (1) serial slice exploration of the ventricular muscle and epicardial coronary arteries; (2) microscopic study of carefully located and oriented blocks of tissue taken from all gross lesions; and (3) following up all the implications of the clinical, electrocardiographic and coronary artery data, in order to suspect or discern very recent damage, evaluate ischemic states not necessarily causing histologic changes, and analyze complex, multiple lesions. We abandoned injection studies of the coronary vessels, except in special cases, because histologic detail was sometimes disturbed by perfusion solutions and delayed fixation, which could prevent recognition of the presence of very recent muscle necrosis.

In part II we discussed the difficulties in describing infarcts, scars and coronary lesions; and also the disadvantages of the conventional methods of illustration. A solution of the problem for individual cases was achieved by (a) accurate drawing of the serial slices with the relevant pathologic data in place, and (b) representation of arterial and muscle lesions and their important interrelationships by myocardial maps of their locations and dimensions. Since the important muscle lesions of human coronary disease are largely confined to the heavy circular ring of left ventricular and septal muscle, especially the layers nearest the left ventricular cavity, our maps were confined to this area, which furnished the additional advantage of permitting concentration of all relevant pathologic data in a single diagram.

Now, in part III, we report studies of 100 consecutive patients selected from the larger series because each had (1) at least one significant coronary narrowing, that is, diminution of the lumen of a major branch to 1 mm. or less at some point; and (2) a recent electrocardiogram, including multiple precordial leads. A fundamental problem appeared to be determining the value of electrocardiography for ascertaining the total ventricular myocardial situation. Because, as our earlier studies had suggested, the tracings at best could give us only parts of a patient’s picture, we realized that our search for types of total pictures could not be started from the electrocardiographic viewpoint. “To what extent is it possible to
correlate the electrocardiographic pattern of patients suspected of having coronary disease with myocardial damage demonstrable at the autopsy?" we had asked in part 1. This question, therefore, had to be approached from the clinicopathologic side.

In short, we decided to see if our data could answer the following questions which must occur to any physician confronted by a patient with myocardial infarction: Is this infarct large or small? What is the condition of the rest of the heart? How much old scarring is there? How much muscle is potentially ischemic and in danger from minor circulatory stress? The two latter questions are of course equally cogent for patients with anginal syndromes or for anyone suspected of having obstructive coronary disease. The attempt to answer all these questions is tantamount to surveying the total ventricular myocardial situation for any particular patient. Concentration upon the coronary lesions themselves cannot answer these questions since the consequence of any given coronary lesion can be determined only by study of the muscle itself.

Our myocardial maps plainly displayed the answers to the questions about infarction and scarring. The ischemic areas were another matter. Estimation of their extent by considering all the coronary and muscle lesions in relation to the clinical and electrocardiographic picture could only be crude, in the present state of our knowledge (see Discussion). When we tried to describe and compare the muscle findings for groups of hearts we were checked by a major semantic difficulty. For patients with coronary disease, conventional terminology altogether ignores describing total ventricular myocardial situations, but is concerned rather with certain limited aspects of particular cases—such as, syndromes (angina, coronary insufficiency), focal pathologic changes (infarction, scar, coronary narrowing or thrombosis), or "localized" lesions ("anterior," "lateral," or "posterior" damage) for the purposes of electrocardiographic diagnosis. So, in order to define, describe and derive conclusions about what our maps were showing us, we were obliged to create a vocabulary. We had to consider not only the age, massiveness and full extent of muscle damage, but also to compare the shapes of lesions with the coronary arterial anatomy. From our specimens the original distributions of the three major arterial trunks, left anterior descending, left circumflex and right coronary (see Methods), had been estimated and were indicated on our maps. When we surveyed the series of patients (only two lacked any muscle damage) in terms of both myocardial damage and original coronary arterial distribution, we found they could be divided into two groups of about equal size: those in which damage could be considered restricted to one of the three major coronary regions, and those in which two or all three regions were involved. For a terminology applicable to the whole series of patients we distinguished "regional damage," that is, damage clearly within the original distribution of a single major coronary trunk, from lesions necessarily of greater extent. The latter we called "widespread damage." This category includes multiple, separate lesions or continuous sheets of damage reaching well into two or all three coronary regions.*

This paper will begin by describing our procedures, including a simple method of charting whereby groups of hearts of any size may be compared with respect to the age, massiveness and extent of lesions and their relationship to the original coronary artery distributions. It enables us to present the data from 100 patients succinctly. This method clearly shows, not only the pathologic anatomy of a segment of human coronary disease, but also the characteristics of the small number of groups, basically different from one another, to which all our patients with myocardial damage could be assigned. The terminology, notation and classification based on this approach permit great simplifications in the description of data, which will make their presentation easier in subsequent parts of our reports, especially the electrocardiographic section† for which this communication will serve as a partial atlas.

* In our initial classification† we used "localized" instead of "regional." Later it became evident that both regional and widespread lesions are localized in the strict sense of the word (see Discussion).
Fig. 1. Hypothetical dissection showing the cardiac anatomy involved in construction of myocardial maps. (a) Heart with atria removed, showing the origins of the three coronary "arteries". A diagonal line indicates the plane of a typical slice, perpendicular to the long axis of the left ventricle. The position of two coronary lesions and an apical scar is indicated.

(b) Cross-section of the human heart at the level indicated in (a) looking down at the apical portion. The similarity in curvature and thickness of the "free" left ventricular walls and their continuation in the septum is shown. The position of anterior and posterior interventricular grooves can readily be seen. Radii have been drawn from the center of the left ventricular cavity. A third radius has been drawn through the center of the lateral wall, opposite the middle of the septum. The drawing will be limited to the left ventricle and septum. The lower edge of a posteroseptal subendocardial scar is shown (lined area).

(c) View of the heart illustrated in (a) after the right ventricle has been cut away along its attachments at the anterior and posterior interventricular grooves. The coronary vessels have been left in situ to illustrate the course of the right coronary artery supplying the posteroseptal region of the left ventricle. The extension of the left anterior descending branch of the left coronary artery to the back of the apex is also shown. The anterior subendocardial scar and septal portion of the posteroseptal scar are visible, as well as a severe narrowing in the distal right coronary artery. The numbered subdivisions of the myocardium are described in figure 2b.

(d) The same specimen as in (c), turned so that the apex is downward, and rotated so that its edges are formed by the midportions of the septum and the lateral left ventricular wall. If the specimen be cut longitudinally down this mid-lateral wall from base to apex it can be opened like a book and the inside of the left ventricular cavity revealed as in (e).

(e) View from the left ventricular side of the opened left ventricular and septal muscle mass. The positions of the anterior descending and the posterior interventricular sulcus coronary branches are shown by dotted lines which thus establish the position of the interventricular grooves. The full extent of the two muscle lesions can now be seen. If cuts be made along grooves from apex to base, the specimen will be divided into three segments. Isometric projection drawings of these segments, after they have been placed with the long axis parallel and the basal portions at the same level, form a useful map of the left ventricular and septal myocardium as illustrated in figure 2.
METHODS

The criteria for selection of cases have been noted. In the evaluation of each heart there were three stages of procedure: (1) dissection, and recording of all relevant data; (2) representation in a single diagram of the ventricular myocardial situation for each heart; and (3) for the present paper, charting together groups of hearts showing broad similarities in type or distribution of muscle damage.

1. Dissection and Recording

(a) The epicardial coronary arteries were explored by multiple cross-sectioning at 2 to 3 mm. intervals. This served both to locate all lesions and to determine the caliber and anatomic extent of the various branches. (b) From the results of the coronary artery exploration estimates were made, for later reference, of the original configuration of the three major coronary regions. (c) The ventricles were fixed in formalin for 24 to 48 hours and then sections (usually 10) were serially cut in planes perpendicular to the long axis of the left ventricle (figs. 1a, b). (d) Blocks for microscopic study were taken from all coronary and myocardial lesions and from muscle areas under suspicion because of narrowing of their regional arteries. (e) Drawings were made of all slices to record their shape, the configuration of gross lesions and the sites of microscopic sections. (f) When all histological data were available, the history and electrocardiographic findings were reconsidered in relation to the anatomic picture. Usually additional questions arose necessitating further microscopic blocks or special staining of those already taken. Once the data were brought to this point, our basic record for each case could be considered complete.

2. Representation of Individual Case Data

(a) A myocardial map was constructed for the individual heart, account being taken of the actual number of ventricular slices and the gross coronary artery anatomy, as illustrated in figure 2a. (b) The maps showed the same landmarks as the serial slices: the interventricular grooves, the mid-lateral wall and the levels of the slices themselves. Consequently the muscle lesions could be transferred accurately slice by slice to the map. Ordinarily only the left ventricle and septum were illustrated, although the right ventricle can be dealt with similarly if desired. (c) The maps were then subdivided into thirds from apex to base, as shown in figure 2a, irrespective of the actual number of slices, which varied somewhat with the size of the heart. These lines of "latitude" were helpful in comparing hearts. They correspond to conventional terminology, e.g. "apical," "middle" and "basal" thirds of the heart. It was also helpful to subdivide the anterolateral and posterolateral segments of the maps into thirds and the septal segment in half by subsidiary lines of "longitude". Thus we had 24 areas comprising the left ventricular and septal myocardium. (d) Special features of particular hearts could also be depicted, such as localized thinning of the wall, position of mural thrombi, and the character of papillary muscle lesions.

3. A System of Notation for Comparing Hearts in Groups

(a) It proved useful to designate certain of the 24 left ventricular and septal myocardial areas as "central" in each coronary region for all hearts. We tried to select those least subject to the effects of anatomic variations.* These "central" areas, shown by heavy outlines on the map in figure 2b, consist of areas 2, 3 and 11 for the left anterior descending coronary region; 21 and 22 for the right coronary region; and 17 and 24 for the left circumflex region. Other areas, commonly within the three regions, designated "probable", are shown by light shading in figure 2b. The remaining areas were considered "uncertain", as we could seldom tell to which of two regions they should be assigned. The common coronary distribution is depicted in figures 1 and 2. (b) Without too much loss of accuracy, each myocardial area could be symbolized by a square. It was then possible to design a linear arrangement of all the 24 areas so that the central and probable areas for each region are kept in groups, separated from each other by the uncertain areas, as in figure 2c. Insofar as possible, areas anatomically adjacent are kept so.† By appropriate symbols the character and amount of damage in each myocardial area could be designated. The charts thus show distribution accurately but indicate amount of damage only approximately, since they exaggerate the size of subendocardial and apical areas.

RESULTS

We plotted the character and amount of damage appropriate to each area as compared with the coronary regions for each of our 44 cases of regional damage (including the two hearts with no damage). Hearts with damage in the same regions were kept together. All the (single) regional lesions were best subdivided into large and small: that is, those involving only a portion of one region and those involving

* The only variant of importance in this regard is a long left circumflex, supplying the branches to the posterior interventricular groove. Nine patients had this coronary artery pattern (the usual pattern in animals) and will be identified in this report.

† A type of frequency diagram that preserves all major anatomical relationships actually was used in evaluating our data.
Fig. 2. Method of mapping and charting ventricular and coronary lesions. (a) Myocardial map of the left ventricle and septum based on their appearance after the hypothetical dissection illustrated in figure 1. While the levels of the actual ventricular slices can be shown in a myocardial map and were in fact used for the accurate transfer of necropy data from slices to maps, it is more convenient for the purpose of this paper, and corresponds well with conventional nomenclature, to consider the ventricle as divided into apical, basal and middle thirds. These form the lines of “latitude” for our map. The lines of “longitude” are provided by the interventricular grooves, the mid-lateral wall, and the middle of the septum. In addition it is useful to subdivide the anterolateral and the posterolateral segments into equal thirds by other lines of “longitude.” Twenty-four subdivisions of the left ventricular and septal myocardium result. The relation of these muscle areas to the main coronary trunks is also indicated by the map. The heart illustrated has the common coronary arterial distributional pattern. The posteroseptal subendocardial scar and the anterior subendocardial scar can now be seen in their entirety. Acute necrosis in the vicinity of the anterior lesion, found on microscopic study, has been indicated by black dots.

(b) Simplified myocardial map of the same heart. Instead of isometric projection drawings, designed to show the edges and three-dimensionality of the myocardial segments, these are now symbolized by shield-shaped figures. The same lines of latitude and longitude are provided as in (a). The same lines are shown, but the thickness of lesions is now indicated only by the type of hatching (key at left). The coronary lesions are also shown by simplified symbols (key at right). The 24 myocardial areas have been given the same numbers seen in figures 1, b c, d and e, and 2a.

This figure illustrates how the numbered areas have been “assigned” to one or another region of supply for each of the major coronary arterial trunks. “Central” areas for each region are blocked out by heavy boundaries. Those myocardial areas probably within the distribution of any particular arterial trunks are lightly shaded. “Uncertain” areas, which might have been supplied in varying measure by either of two major coronary trunks, are left unshaded. The arrows and shaded zones show how the “central,” “probable,” and “uncertain” areas are related to the linear display below (c). Note that the greater simplicity of the two-dimensional shield-shaped drawings of the ventricular segments is at the expense of some distortion. The actual extent of the inner layers of the left ventricular and septal muscle is considerably less than the outer layers, as the isometric projection drawings indicate.
most of the region, including even some “probable” areas in adjacent regions. The results are shown in figures 3 and 4. The 56 hearts with widespread damage could be charted similarly. They also fell into two groups. In 36, the definitive lesions—the earliest that established the presence of widespread (bi- or triregional) damage—consisted of healed scar in the central areas of two regions. The remaining 20 patients were entitled to place in the “widespread” category only because of acute damage in the central areas of two regions, although some had had small amounts of old scarring in one region. We called these two subdivisions “widespread scar” and “widespread acute infarction”. They are shown in figures 5 and 6.

1. Survey of Four Basic Ventricular Myocardial Situations

(a) Figure 3 shows all the hearts with small, single, regional lesions: group I. The predominantly subendocardial character of the damage (hatching) is apparent, as is the relatively limited extent of the lesions. A conspicuous feature of this group is the extent to which the anterior descending coronary artery region has been spared (see part 4). There was about an equal frequency of damage in the distributions of the right coronary artery and the circumflex. Occasionally it was not easy to decide whether a small lesion should be assigned to the right or the circumflex regions. We have rigorously based our final regional classification on the central areas aforementioned provided these were actually involved. (See legend, fig. 7.) One patient had strictly a right ventricular infarction, the only example of damage confined to this chamber. The two hearts without muscle damage are charted just below group I.

The coronary lesions of group I are also shown in figure 3, differentiation being made among narrowing, old occlusion and recent thrombosis, with or without a pre-existing narrowing. It will be noted that more than one-third of the group had only one coronary artery narrowed or occluded. However, the remainder, indistinguishable from the others so far as muscle lesions were concerned, had two or all three major arterial trunks partially or completely occluded. Recent thrombi were uncommon (20 per cent in this group and recent muscle damage the exception (36 per cent), half of the latter consisting of acute necrosis in the vicinity of ancient scars.

(b) Figure 4 depicts the muscle damage found in all the hearts having large regional lesions. These patients constitute group II. The tendency of massive lesions to spread into the border (“probable”) areas of the other coronary regions is clearly shown. However, it can be seen that the central areas were not involved by massive damage (solid black or double cross-hatching) in more than one arterial region for each patient. There were, surprisingly, no true “lateral” infarctions of this massive, regional type although many of the large regional anterior lesions involved the apical third of the lateral wall and even its middle third. Myocardial rupture occurred in only one, case 3.

The coronary lesions of these patients were characterized by there being invariably a recent thrombus in the proximal portion of the regional artery for every acute infarct, usually associated with a previous severe narrowing of the vessel. However, only three patients failed to have severe narrowings or occlusions, old or recent, in two or even all three of their major coronary vessels. Right ventricular damage was common as an extension to the

(c) Linear rearrangement of the 24 myocardial areas. For simplicity all areas are represented by squares. This somewhat enlarges the eight apical areas, which contain less muscle than the other sixteen areas. Notations below the display relate the areas to conventional anatomic nomenclature. In each square the approximate extent of damage is shown, beginning with old scar, if any, at the bottom of the square and then any acute separate damage. Acute damage when present at the site of old scar is indicated by a large black dot, but without an attempt to express variations in extent. Ages of scars are not symbolized.
anterior wall from anterior lesions, and to the diaphragmatic surface from posteroseptal lesions. Mural thrombi in both the right and the left ventricle were also common. Important anatomic variants of coronary supply were common only in group II: a large left circumflex and short right coronary being found in five patients with anterior coronary regional damage.

(c) Figure 5 shows the “widespread scar” patients of group III. No differentiation is made here for the ages of scars. Three characteristics should be noted. (1) The typical lesion was subendocardial scarring (hatching), usually quite extensive, involving the central areas of two or all three coronary regions. Transmural scar was uncommon. (2) Acute damage was common but extremely variable in its character. Sometimes it consisted of transmural and sometimes of subendocardial damage: most often mixtures of acute damage and scar in the same area. (3) In the corresponding coronary artery an acute thrombus was often present, but the uniform finding was old ob-

**Fig. 3.** The total myocardial damage picture of the 22 patients with small regional lesions and two in whom no damage was found at necropsy. Symbolism is the same as in figure 2c. The numbers on the left-hand side are for convenience of reference to particular cases. Actual case numbers are on the right of the arterial lesion symbols. A short right coronary artery (large circumflex) was present in case 22.
ARTERIAL CONSTRUCTION (severe narrowing or occlusion) of two or all three of the main coronary arteries.

(d) Figure 6 shows the “widespread acute infarction” patients of group IV. Three characteristics should be noted. (1) The common, prominent lesion was acute subendocardial infarction (checkered symbol). Acute damage was invariably widespread, involving the central areas of at least two regions in all but two instances. These had central area infarction in only one region, but damage involved the “probable” areas of all three coronaries in patterns indicative of bi-regional damage (cases 2 and 4). Damage tended to be more extensive and massive in hearts that had previously been scarred, these often being associated with an area of acute transmural damage (solid black) that might be slightly later in date. (2) When scar was present it was subendocardial, small in extent, and limited essentially to one region. (3) The characteristic coronary artery lesion was severe narrowing or old occlusion of two or all three of the major coronary trunks. It was common (60 per cent) to find recent thrombosis of a previously narrowed coronary artery, although this was not always the artery that appeared to have supplied the areas of most intense acute myocardial necrosis (cases 12, 13 and 18). In one instance, two recent thrombi were found. One patient’s left main coronary artery was the seat of a recent thrombus. These, however, were very unusual situations that did not occur in the other groups.

Fig. 4. The total myocardial damage picture for 20 patients with large regional lesions at necropsy. Symbolism is the same as in figure 2c, and the legend to figure 3. A short right coronary artery (large circumflex) was found in cases 8, 9, 11, 14, and 19. In case 5, scar extended into a portion of one central area for the circumflex region, but the lesion was thought to be basically uniregional and is assigned to the right coronary region.
(e) The four basic groups differed considerably both in behavior during life and in manner of death. Only a few of the patients with a small localized lesion (group I) were subject to the anginal syndrome. When death occurred in the presence of such minimal damage, it was due to ‘noncoronary’ factors such as cerebral vascular lesions, or, in some hypertensive patients, to left ventricular failure.

In many patients with large localized lesions (group II) large acute infarctions befell the victims unheralded, or were preceded by only a short period of anginal distress. Once healed, these large lesions were seldom followed by
significant further damage. Sequelae of left ventricular failure, with or without embolism, were not infrequent. Some patients were almost asymptomatic, and died of unrelated conditions.

The order of events could often be discerned best from the historical and electrocardiographic data available for the majority of the widespread scar patients (group III). Two or more healed lesions, differing in histologic age, usually could be defined at necropsy, although a minority of the patients had widespread scar sheets not readily separable into areas of different histologic age. However, even in these latter hearts there was usually one separate older or more recent scar demonstrating the episodic character of at least some of the damage. Congestive heart failure was fairly common in this group, but "one more" terminal infarction was often the major cause of death.

The patients with widespread infarction (group IV) tended to have had frequent severe anginal pain attacks on relatively slight provocation, sometimes for years prior to the development of acute infarction. Sudden death was common. Often the clinical pictures suggested that infarction had been precipitated

Fig. 6. The total myocardial damage picture of 20 patients with widespread acute infarction at necropsy. Symbolism is the same as in figure 2c and the legend to figure 3. Two recent thrombi occurred in case 7. In case 20 there was a recent thrombus in the previously-narrowed left main coronary artery at the site of a broken plaque, and one of the major divisions of the anterior descending coronary artery was occluded by atheroma (not indicated). The lateral scarring in case 13 was thought to be still in the right coronary region; otherwise the heart would have been classified with group III: A large circumflex (small right coronary artery) was found in cases 4 and 17. Both these hearts contained very early damage, the full extent of which was thought to be considerably greater than that recorded.
by acute anemia or blood pressure falls due to some unrelated disease.

2. Analysis of Series by Lesions in Coronary Regions and Major Arteries

Certain general characteristics of our sample of coronary disease can be quickly grasped if attention is first given only to the damage in central areas for each region. The upper bar graphs of figure 7 provide a summary of the type and frequency of central area damage by regions. It can be seen that subendocardial scarring was by far the commonest type of damage, occurring in 65 per cent of the patients (112 regions). Acute transmural infarction was next in frequency; in 28 per cent of the hearts (32 regions). A transmural portion of lesion that was large enough to involve “central” myocardial area led us to clas the whole lesion as “transmural” for the reg in this bar graph summary. Acute subendo
cardial infarction and acute damage in vicinity of old scar were equally common, occurring in 16 per cent of the patients and 25 regions respectively). Transmural was the least frequent type of damage, be found in 14 per cent of the patients (and regions). It was common only among the re
gional scars of the patients of group II.

From figure 7 it can also be seen that “c coronary obstructions—occlusions or severe stenoses—were together overwhelmingly

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**Fig. 7.** Comparison of the muscle and coronary lesions in 100 patients having at least one severe coronary narrowing. The upper bar graphs denote myocardial damage in the central areas of each of the three major coronary regions. When the central area was spared, damage present in probable areas for the artery concerned was recorded except when it was considered to be an extension of a lesion lying mainly in an adjacent coronary region. Since the patients in groups I and II had damage limited to one region, by definition, the total height of the bar graphs for each of these groups equals the number of cases in the group. In the other groups there was always muscle damage in two or more regions at necropsy. Consequently the bar graph lengths total much more than the number of patients in the groups (compare fig. 8). Lesions in the coronary arteries supplying the major regions are summarized in the lower bar graphs.
commonest type of arterial lesions in the series. They involved each of the three coronary arteries with about equal frequency. Recent coronary thrombosis at a previously narrowed site was the next most common lesion. Recent thrombosis without severe pre-existing stenosis was less common still.*

Coronary obstructions were, indeed, far commoner than muscle lesions. This relationship is more easily seen when only the old muscle and coronary lesions are considered. Comparison of the hatched and cross-hatched portions of the upper bars and the "empty" portions of the lower bars in figure 7 gives a picture of the relative incidence of scar and obstruction presented by our series of patients before any of the acute infarcts or recent thrombi had appeared. It can then be seen that in group I, 61 per cent of the 66 major arterial trunks were obstructed. In group II, 55 per cent of the 60 major arterial trunks showed one or more old obstructions. In group III the incidence of old obstruction was 83 per cent for all three arteries, while in group IV it was 91 per cent.

Now, since our criteria for selecting the patients necessitated every heart having one arterial occlusion or severe narrowing, we must expect at least 33 per cent incidence of old obstruction and or recent occlusion for the 126 major arteries in the regional damage groups (I and II). Furthermore it so happened that we never found scar without at least one severe narrowing in the regional artery. Thus in group III, with old damage in two or all three coronary regions, an incidence of old occlusion or severe narrowing might be expected in over 67 per cent of the 108 major arterial trunks. In group IV, with the great bulk of damage recent, the frequency of old coronary obstructions again need not have been higher than 33 per cent despite the presence of 12 small regional scars.

* It should be noted that one of the systematic errors of even a thorough autopsy is to exaggerate the number without narrowing because of failure to take a section through the narrowest portion of a thrombosed artery. (See part V.)

3. Combinations of Muscle Lesions. Interrelations Among the Basic Groups

A comparison of the scar patterns (lesions at least a month old) with the total damage pictures at necropsy is given for the central areas of all patients in the bar graphs of figure 8. For groups III and IV the combinations of regions damaged are shown. Examination of our data in this form may throw light on interrelations among the basic groups and their natural history, as well as the structural basis for diagnosis in our sample prior to the development of myocardial situations that at necropsy were found to be in an acute or subacute stage.

A striking feature is that one out of four patients had an anatomically undamaged heart muscle prior to the terminal episode of infarction: 11 patients in group II, eight in group IV and four in group I, in addition to the two patients who had never had any muscle damage. Furthermore 30 additional patients, the remainder of groups I and IV, had damage in only one region or a part thereof. Yet the incidence of old coronary obstructions was much higher than expected for both the unscarred and the (small) regionally scarred hearts, as reference to the basic data in figures 3, 4 and 6 will show. Obviously, individual cases could not have been distinguished on the basis of the pattern of coronary narrowings and old occlusions alone.

Comparison of the upper with the lower bar graphs of figure 8 make it clear that the scar patterns alone would have been an inadequate basis for prognosis even if the presence and configuration of all scars were ascertainable. For example, the patients with no scar met at least three entirely different fates during the last month of life, as is shown in the lower bar graphs. There was, moreover, comparatively little difference in the lesions ultimately found at necropsy between certain patients with small regional scars and those with none, for both could develop terminal widespread acute infarction, as in group IV. On the other hand, small regional scars were common both in patients destined to suffer widespread terminal infarction and those in whom any acute
necrosis remained subregional and was considered only a contributory cause of death.

The descriptive names we have chosen for the groups, based as they are on muscle damage alone, can therefore be assigned to some of them at necropsy only. It can be seen from figures 7 and 8 that groups I and IV would have been indistinguishable on the basis of their muscle scars, although there was a statistically higher frequency of old coronary narrowing and old occlusions in group IV.

The group III, "widespread scar," patients of course conformed to the same definition prior to the superimposition of recent damage. In group II the old scars were essentially unchanged, all of the large acute regional lesions developing in patients who had no previous muscle damage. Thus, at best, the scar patterns would have permitted classification of not more than 45 per cent of our patients had we been able to know the actual type and distribution of the damage. To have known whether the other 55 per cent had no damage or a single, small, regional scar would have been of little help so far as prognosis was concerned. It was characteristic of these patients that only their patterns of terminal acute damage revealed the extent and character of the low-threshold, localized ischemic areas that we believed represented the fundamental physiological difference between the groups. (See Discussion.)

While undamaged hearts became more common as we viewed the sample without charting any acute damage, certain myocardial situations remained surprisingly scarce. We still

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**Fig. 8.** Comparison of healed and recent myocardial damage in 100 patients. The upper bar graphs show the frequencies of healed scar in each of the three coronary regions of the statistical series of patients. The bar graph incidence refers to damage in central areas only, with the occasional exceptions described in the legend to figure 7. For groups I, II, and IV, in which all scarring was essentially regional, the affected regions are plotted separately. In group III, where by definition scarring was present in two or all three regions, the damage is plotted so as to show the combinations of regions affected. As shown, 25 hearts would have contained no myocardial damage 30 days before death. The lower bar graphs complete the picture of central area damage for the whole series of patients by adding the lesions that appeared during the last 30 days of life. For groups I and II the bar graphs, identical with those in figure 7 except for the change in scale, are for comparison. Groups III and IV have their total damage pictures plotted in terms of combinations of regions. Throughout, the total height of the bars or combinations of bars for each group is equal to the total number of patients in each group. Thus the whole of the present figure reflects case incidence of damage.
found almost no small healing regional lesions (15 to 45 days old). Obviously all the small regional scars must have been in such a state at some time, but the chances of finding exactly this condition at necropsy would be small unless the patients were killed primarily by the infarctions in question. Furthermore the combination of one small regional scar with a healing small regional lesion was rare, presumably for the same reason. Most of the scarred hearts in group III must have had such a combination of lesions at some time, although we could not be sure that a few of the widespread scar sheets might not have been due to the healing of widespread subendocardial infarctions. Our data obviously do not justify the inference that lesions of this latter type must always be lethal.

Review of figures 7 and 8 enables us to make certain inferences concerning the order of development of coronary obstruction and ventricular muscle damage insofar as human coronary disease is exemplified by our series of patients. Coronary narrowing appeared to be the precursor of almost all the muscle damage we found, whether that damage resulted from gradually increasing stenosis, from circulatory stress, or was associated with coronary thrombosis at the narrowed point. Although only two hearts in this series had no muscle lesions at necropsy, there seems to be little doubt that narrowing without regional muscle damage is a common situation during life but seldom found at necropsy because it is rarely lethal. Certainly it must have existed in one-fourth of our patients a few weeks before they died. Old coronary obstruction (narrowing or occlusion) without muscle damage also must have been the precursor state for all the patients with small regional scars in groups I and IV.

The combination of one small, regional subendocardial scar and one healing, regional infarction elsewhere in the heart would provide a picture transitional between the small regional lesions of group I and the multiple or widespread lesions in group III. It could scarcely be doubted that many of our widespread scar patients at one stage must have been developing their muscle damage picture in such a manner. We have, however, rarely seen hearts with one small regional scar plus a separately placed acute, small infarction confined to a second region at necropsy, and no instances occurred in the basic series.

It has already been mentioned that the "widespread infarction" hearts of group IV that had scarring would have been almost indistinguishable anatomically, prior to the development of their terminal lesions, from the small regional scars of group I, although the degree of coronary stenosis tended to be more severe in group IV. Thus, a group I anatomic picture upon occasion may be a precursor state for group IV. Although it is possible that a group I state might be a precursor for occasional patients of group II type (with a healed lesion formed by repeated infarctions all within one coronary artery's distribution), we have elicited no definite evidence that such a relationship had existed in any of our cases. Obviously certain transitions between the groups would be impossible. Scars do not disappear and their presence limits the possible transitions for those hearts.

4. Peculiarities of the Frequency and Anatomic Location of the Common Types of Muscle Damage

Because there was little difference in the overall incidence of coronary lesions among the three major regional arteries, it might be expected that damage in each of the three regions would not differ greatly in type or frequency. This was not so. (a) Small, isolated anterior regional lesions were rare, whereas small isolated right or circumflex regional lesions were common. (b) No large isolated circumflex regional ("lateral") infarcts or scars were found at all. (c) Among the widespread damage hearts, the combinations of damaged regions that included the central areas of both the anterior and the right ("posterior") coronary regions were much commoner than the other combinations.

(a) When anterior regional lesions occurred alone, they were common only as the massive infarcts and scars of group II. There were, indeed, three times as many of the latter as posteroseptal lesions of the same type. In contrast, almost every other lesion affecting
the anterior region was part of a widespread or “multiple-region damage” situation. Since small regional lesions were fairly common it followed that these were in the right or left circumflex coronary distribution almost invariably: that is, “posterior”, “posteroseptal”, “posterolateral” or “lateral” in their location. This was true not only of the small regional lesions of group I: almost all the old lesions found in the majority of the “widespread acute infarction” hearts of group IV were also small and regional. Furthermore, less than one fifth of the hearts with widespread healed damage (group III) presented clear-cut evidences that the anterior coronary region had been involved before the others, while the majority could be shown to have had pre-existing damage in the right coronary or the left circumflex regions, or both, as their initial ventricular muscle lesion. The widespread acute infarcts of group IV, however, appeared to affect any two of the three regions with comparable frequency. Thus, with the exception of the large regional lesions (group II), and the minority of group IV in which the first damage to the heart was widespread infarction, muscle damage in the left ventricle tended to begin in regions other than the anterior.

### Table 1.—Salient Anatomic Characteristics and Certain Clinical Features of the 4 Basic Myocardial Damage Groups

<table>
<thead>
<tr>
<th>Characteristic muscle lesions</th>
<th>Group I (22 cases) Small, Regional Lesions</th>
<th>Group II (20 cases) Large, Regional Lesions</th>
<th>Group III (36 cases) Widespread Scar</th>
<th>Group IV (20 cases) Widespread Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single subendo-cardial scar, acute damage sometimes intermingled. Rarely one regional subendo-cardial acute infarction</td>
<td>Transmural damage: scar or acute infarction, usually not both</td>
<td>Subendocardial scarring; multiple lesions or a widespread sheet. Commonly a terminal acute lesion also</td>
<td>Acute subendocardial infarction. Transmural portion occasionally. Scar small and regional or absent. Two recent lesions rare</td>
<td></td>
</tr>
<tr>
<td>Anterior coronary region spared. Damage posterior or lateral mainly</td>
<td>Heaviest at apex or posteroseptal region of left ventricle. Right ventricular extensions common</td>
<td>Scar almost anywhere in left ventricle or septum. Earliest lesion usually posterior or lateral. Acute damage at scar sites or separate</td>
<td>Variable distribution. Sometimes too recent to be mapped in detail. Scar posterior or lateral, if any</td>
<td></td>
</tr>
<tr>
<td>Uencommon (19%)</td>
<td>In artery supplying any acutely infarcted area</td>
<td>One in 61%</td>
<td>One in 65%. Sometimes not in “expected” artery. Rarely two</td>
<td></td>
</tr>
<tr>
<td>One or more arteries. Single artery in 50%</td>
<td>One or more arteries. Single artery in 35%</td>
<td>Two or more arteries</td>
<td>Two or more arteries</td>
<td></td>
</tr>
<tr>
<td>Angina sometimes. Death not directly due to muscle damage or ischemia</td>
<td>Short history or none. Death from effects of acute infarction, embolism or left ventricular failure</td>
<td>Long histories. Multiple episodes of clinical “acute infarction”. Failure common</td>
<td>Severe anginas; sudden deaths. Precipitation of infarction by acute exertion, anemia, or hypotension</td>
<td></td>
</tr>
<tr>
<td>Little changed. One small scar, rarely no damage</td>
<td>No lesion or a single large, regional scar</td>
<td>Relatively little change, but slightly less damage</td>
<td>No lesions or one small, localized scar</td>
<td></td>
</tr>
<tr>
<td>Coronary obstruction without muscle damage</td>
<td>Coronary obstruction without muscle damage</td>
<td>Small, regional lesion, as in Group I</td>
<td>Group I (if scar); coronary obstruction without damage</td>
<td></td>
</tr>
</tbody>
</table>
(b) The low frequency of large circumflex regional ("lateral") lesions has already been mentioned in the description of group II. Lateral damage was seen only as small, regional scars or as part of a widespread damage situation. In the latter circumstance almost any type of lateral wall involvement could be expected. These peculiar relationships are summarized in figure 7.

(c) The widespread damage combinations graphed in figure 8 also show a much higher incidence of anterior-plus-right-coronary-region damage and of damage in all three regions, as compared with either anterior-plus-circumflex or right-coronary-plus-circumflex-region damage. Thus, we can say that circumflex region ("lateral") damage, common in hearts with widespread lesions, was much more often found in association with both right and anterior coronary region damage than with either one alone. To state the same fact in another way: the combinations of damaged regions that included the "whole" septum were remarkably common in both widespread damage groups. It was uncommon to find combinations in which either the septum's posterobasal area (case 21, supplied by the right coronary) or its anterior apical areas (cases 4, 5 and 12, supplied by left anterior descending) were anatomically intact.

We have observed no correlation between these peculiarities of lesion location and combination, and the location of disease in the individual coronary vessels. The frequencies of old lesions in the major regional arteries were much the same, as figure 7 shows. The over-all frequency of severe narrowing or old occlusion was 82 per cent for the left anterior descending, 79 per cent for the right coronary artery, and 80 per cent for the left circumflex. Recent thrombi had only one third the frequency of old lesions. They were less frequent in the left circumflex than in the other two major regional arteries.

The salient features of the myocardial situations described so far are summarized in table 1.

(To be concluded in the October issue)
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
JOHN J. SAyEN, WARNER F. SHELDON and CHARLES C. WOLFERTH

doi: 10.1161/01.CIR.12.3.321

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:
http://circ.ahajournals.org/content/12/3/321.citation

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