Subendocardial Infarction: Report of Six Cases and Critical Survey of the Literature

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In the ordinary evolution of an acute myocardial infarct the electrocardiogram shows T wave (ischemia), RS-T segment ("current of injury") and QRS (death of muscle) changes. This paper presents a special group of cases of infarction in which only T wave and RS-T segment changes developed even when patients were observed over a considerable period. Therefore, the curves as such could not be considered diagnostic of myocardial infarction. The authors here describe a unique and intriguing group of cases of fatal myocardial infarction with electrocardiograms resembling those seen in stress tests for coronary insufficiency and showing rimlike subendocardial infarcts at postmortem.

It is now quite generally recognized that acute transmural infarcts of circumscribed distribution and resulting from inadequacy of the flow of blood through one of the major coronary branches may be accurately detected and localized electrocardiographically. Initially these were regarded either as anterolateral or posterobasal in distribution, but with the development of the multiple chest lead technic and unipolar electrocardiography it has become possible to recognize anteroseptal, anterolateral, posteroseptal, and similarly located infarcts. It is also known that, classically, these zonal transmural infarcts are roughly wedge-shaped with the base of the wedge toward the endocardium. Recent isolated studies,1-6 however, have demonstrated the feasibility of recognizing myocardial infarcts which are principally limited in distribution to the subendocardial layers of the myocardium.

In the investigation of 150 consecutive individuals who were studied at least once during their terminal illnesses by means of a multiple unipolar electrocardiographic technic, and who were subsequently examined post mortem,7 6 individuals were found with infarction of this type among 65 with myocardial infarction. It is the purpose of this article to present this group of 6 cases of subendocardial infarction confirmed at autopsy and to discuss the relevant literature.

Case Reports

Case 1. (P.B.B.H., 7A850). S.L., a 53 year old shipper with syphilis and angina pectoris, was admitted to the Peter Bent Brigham Hospital on March 15, 1948, because of severe substernal pain of four days' duration. Physical examination showed the patient to be in shock with a heart rate of 104 and an unobtainable blood pressure. The electrocardiogram (fig. 1, A) showed depression of the RS-T segments in Leads I, II, aVR, V6, and V4 and elevation of the RS-T segments in Leads aVR and V1 to V6; there was no Q wave in Leads III or aVF. These tracings were interpreted as very suggestive of subendocardial infarction of the left ventricle. The patient died three hours after admission to the hospital.

Postmortem examination showed the characteristic findings of syphilitic aortitis with marked narrowing of the coronary ostia. Except for a few small yellowish plaques, the coronary arteries were normal. The heart weighed 380 grams, was removed in toto, and fixed. Following fixation in formalin it was sectioned transversely at 1-cm. intervals from the apex to the atroventricular sulcus. This technic was used in all but one of the cases described in this article. In cross section (fig. 1, B) the wall of the left ventricle was seen to consist of three concentric layers. The outer (subepicardial) layer consisted of normal-appearing myocardium. The second, middle layer, consisted of pale, firm myocardium averaging 1.2 cm. in thickness. Both of these layers appeared normal microscopically. The pallor can be accounted for by fixation artifact. The inner (subendocardial) layer, measuring 0.2 cm. in thickness, was purple in color and of a soft consistency. This layer demonstrated the changes of myocardial infarction of seventy-two to ninety-six hours' duration.

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Fig. 1.—Subendocardial Infarction with Syphilitic Ostial Disease (Case 1).

A. Tracing shows depression of RS-T segments in Leads I, II, aV₁, aV₅, and V₄ to V₆; elevated RS-T segment and late inversion of the T wave in aVR suggest injury orientated toward the ventricular cavity. The depressed RS-T segments in V₄ to V₆ suggest either subendocardial infarction or transmural posterior infarct but the latter is unlikely because of the absence of a Q wave in Lead aVF. B, Transverse section of the heart between the apex and the atroioventricular sulcus (midway). Note the subendocardial rim of dark, infarcted muscle corresponding to the distribution of the subendocardial portions of the superficial sino- and bulbospiral muscles. The posterior papillary muscle is also infarcted. (1, Left ventricle; 2, right ventricle; 3, anterior; 4, posterior; 5, infarcted zone; 6, infarcted posterior papillary muscle.) C, Low-power photomicrograph of myocardium showing pale rim of normal-appearing myocardium separating the endocardium from the infarcted area and sheathing the infarcted trabeculae carneae. Note small patent coronary vessel in the epicardial fat. (1, Epicardium; 2, endocardium; 3, infarcted zone.)
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according to the criteria of Mallory and associates. Further microscopic examination (fig. 1, C) revealed a zone of relatively intact myocardium, 0.5 mm thick, immediately beneath the endocardium separating it from the infarcted myocardium. The infarcted area extended from the base to a point midway from the apex and was most extensive at a point 5 cm from the apex.

In this case the upward RS-T displacement in leads from the right side of the precordium and the downward displacement in the leads from the left side would also be consistent with anteroseptal infarction. It is possible that, had the patient lived longer, he might also have developed QRS changes. The lack of distinct QRS changes might also be explained as the result of subendocardial infarction, particularly if prolonged electrocardiographic observation fails to reveal the development of QRS changes while collateral clinical evidence of infarction is present. In the patient of Alzamaora, almost duplicate conditions existed. Each had syphilitic narrowing of the coronary ostia, each showed a similar unipolar electrocardiographic pattern (depression of the RS-T segment over the precordium, elevation of RS-T in aVR, and no significant Q wave in aVF) and each showed infarction limited to the subendocardial strata. The patient with subendocardial infarction reported by Pirani and Schlichter, who had narrowing of the coronary ostia by calcific plaques and a positive serologic reaction for syphilis, almost certainly belongs in the category with these two cases. The electrocardiogram of this patient, employing CF leads, showed depression of the RS-T segment in Leads I, II, CF, and CF which was considered characteristic of so-called left ventricular strain.

Case 2. (P.B.B.H., 7A918). E.L., a 58 year old housewife with long-standing diabetes mellitus, arteriosclerotic heart disease, and congestive heart failure, was admitted to the hospital while suffering an attack of myocardial infarction. Physical examination showed the patient to be in shock, with tachypnea (respirations 40 to the minute). Her skin was ash-gray in color. The electrocardiogram (fig. 2, A) showed a prominent T wave, depressed RS-T segment, and biphasic T wave in Lead I; a depressed RS-T segment and inverted T wave in Lead II; and a T wave in Lead III which was low and biphasic. The unipolar limb leads showed an elevated RS-T segment with upright T wave in aVR, depressed RS-T segment and biphasic T wave in aVF, and absence of a prominent Q wave in aVF. The unipolar chest leads showed slight depression of the RS-T segments in Leads V, and V, biphasic T waves in V, and V, and inverted T wave in V, the transitional zone was between V, and V. These tracings were interpreted as consistent with acute cor pulmonale; subendocardial infarction was considered but thought less likely. Tracings on the following day showed no further change. The patient died three days later.

Postmortem examination showed cardiac enlargement (the heart weighed 650 grams) and severe coronary sclerosis, but no fresh thrombus was found. The heart was fixed and sectioned in the manner described for Case 1. The endocardial half of the posterior wall of the left ventricle showed purple laminations which extended well to the posterolateral angle and to the posterior half of the interventricular septum; there were small focal patches of similar discoloration in the endocardial one-third and papillary muscles of the anterior wall of the left ventricle, best seen near the apex (fig. 2, B). Microscopic examination showed these areas to exhibit the features of a three-week old infarction with a normal-appearing zone of myocardium 0.3 mm thick immediately beneath the endocardium. There was no pulmonary embolism or infarction.

In this case the electrocardiographic diagnosis of acute cor pulmonale was favored over that of subendocardial infarction although the latter was considered. Master and his collaborators described a case which is quite the reverse, that is, one in which the tracing resembled subendocardial infarction but in which acute cor pulmonale was found at autopsy. Büchner described coronary insufficiency with focal necrosis distributed under the endocardium of the right ventricle resulting from pathologic overloading of the right ventricle produced in experimental pulmonary embolism. There is good evidence for impairment of coronary blood flow in acute cor pulmonale but at present it is not known with certainty which part of the myocardium suffers most from this impairment. Insofar as right ventricular pressure is raised, one might expect a decrease in the blood supply to the right ventricle but this wall is thinner, its arteries enter the muscle on a straighter course than do those entering the left ventricle, and the deeper layers are closer to their nutrient vessels. It seems possible, therefore, that acute cor pulmonale and
subendocardial ischemia or infarction are not necessarily incompatible conditions and may at times coexist. At present adequate data to answer this question are not available and we can merely propose the problem.

Leads I and II. The unipolar limb leads showed depression of the RS-T segment in aVL and biphasic T waves in aVL and aVF. The unipolar chest leads showed tall R waves, depressed RS-T segments, and inverted T waves in V₅ and V₆ with slight elevation of the RS-T segments in V₁ and V₂. There

Fig. 2.—Subendocardial Infarction Resembling Acute Cor Pulmonale (Case 2).

A, Tracings show a prominent S wave, depressed RS-T segment, and biphasic T wave in Lead I; depressed RS-T segment and inverted T wave in Lead II; low biphasic T wave in Lead III; elevated RS-T segment and upright T wave in Lead aVR; biphasic T wave in aVL; slightly depressed RS-T segment in V₄ and V₅. The Q wave is present but not prominent in aVF.

B, Transverse section of lower half of the heart showing a circumferential rim of infarcted myocardium, most prominent posteriorly, involving papillary muscles. (1, Left ventricle; 2, right ventricle; 3, anterior; 4, posterior; 5, infarcted zone; 6, infarcted columnae carnæ.)

Case 3. (P.B.B.H. 179739). A.P., a 61 year old piano-maker with pernicious anemia, was admitted to the hospital because of an attack of myocardial infarction. On admission his blood pressure was 146/80. The electrocardiogram (fig. 3, A) made eighteen hours after admission, showed an abnormal form of the ventricular complex with slight depression of the RS-T segments and biphasic T waves in were frequent ventricular premature beats and auricular premature beats. These changes were interpreted as characteristic of left ventricular hypertrophy. The patient died on the following morning. A second electrocardiogram had not been made.

The significant findings at postmortem examination were limited to the heart. This organ weighed 440 grams and showed thickening of the left ven-
Fig. 3.—Left Ventricular Hypertrophy Possibly Masking the Electrocardiographic Evidence of Subendocardial Infarction (Case 3).

A, The tracings show depressed RS-T segment in Lead I, left axis deviation, depressed RS-T segment in aV<sub>L</sub>, biphasic T wave in aV<sub>L</sub>, elevated RS-T segment in V<sub>1</sub> to V<sub>3</sub>, tall R wave in V<sub>1</sub> and V<sub>5</sub>—features characteristic of left ventricular hypertrophy. No superimposed changes suggested infarction. (These tracings may not have been made at the time of the terminal infarction.) B, Transverse section through ventricles. Note old posterior scar extending laterally. There is a purple rim of infarcted myocardium extending around the entire circumference of the left ventricle confined to the inner one-third of the left ventricular wall and involving the papillary muscles. (1, Left ventricle; 2, right ventricle; 3, anterior; 4, posterior; 5, infarcted zone; 6, infarcted posterior papillary muscle; 7, old posterior scar.) C, Low-power photomicrograph showing dense scarring immediately subendocardial and the subjacent patchy necrosis limited to the inner one-third of the thickness of the wall. (1, Epicardium; 2, endocardium; 3, infarcted zone beneath scarred area.)
tricular wall. The coronary arteries were markedly sclerotic throughout with striking reduction of caliber of the lumen but no antemortem thrombus was seen. The heart was sectioned as previously described. The posterior wall of the left ventricle was the site of an old white myocardial scar which was transmural in distribution and which extended around the left lateral aspect of the left ventricle with a subendocardial distribution (fig. 3, B). In addition, a rim of left ventricular muscle next to the endocardium varying in width from 1 to 3 mm. was the site of purplish discoloration; similar areas were seen in the papillary muscles of the left ventricle. These changes were circumferential involving the nonfibrotic portion of the myocardium. Microscopy (fig. 3, C) showed the white areas to be healed myocardial infarction which was transmural and the purple areas to be subendocardial areas of acute infarction of less than twenty-four hours' duration.

In this case the electrocardiogram showed changes of left ventricular hypertrophy while autopsy showed an old posterior myocardial infarction and a very recent subendocardial infarction. Autopsy experience has shown that old posterior myocardial infarction may very easily be missed electrocardiographically especially in the presence of left ventricular hypertrophy. Since depression of the RS–T segments over the left precordium occurs in left ventricular hypertrophy it would be conceivable that the superimposed development of fresh subendocardial infarction might be missed because the electrocardiogram had already shown RS–T depression. However, since the tracings were made more than twelve hours before exitus, it seems possible that, had tracings been made during the two hours ante mortem, changes of subendocardial infarction might have been revealed. Nonetheless, it would seem that, in some cases, the changes of acute subendocardial infarction may be masked by pre-existent left ventricular hypertrophy. A similar situation was noted in Case 5 (below) and in the case described by Pirani and Schlichter.

Case 4. (P.B.B.H., 8A459). A.A.C., a 48 year old manufacturer, with a history of angina pectoris and one attack of myocardial infarction three years previously, was admitted to the hospital because of a fresh attack of infarction associated with syncope. The electrocardiogram (fig. 4, A) showed complete A-V block with an auricular rate of 94 and a ventricular rate of 42 beats to the minute. There was marked depression of the RS–T segments in Leads I, aVL, and V₁ to V₅; marked elevation of the RS–T segment in Leads II, III, and aVF, there being almost monophasic action curves in the latter two leads. The Q wave was absent in Lead II and rather small in Leads III and aVF. In spite of the absence of deep Q waves at these points, the tracings were regarded as evidence of acute posterior myocardial infarction.

Shortly after admission to the hospital the patient went into shock, and expired twelve hours following admission.

At postmortem examination the heart weighed 400 grams. The coronary arteries were found to be quite sclerotic and tortuous and showed many areas of markedly reduced caliber, most obvious in the branches of the left coronary artery. A fresh thrombus completely occluded the left anterior descending coronary artery 2 cm. from its origin. The right posterior descending coronary artery was the site of an old recanalized thrombus 8 cm. from the origin of the artery. The heart (fig. 4, B) showed laminated scarring in the posterior wall of the left ventricle 4 cm. in diameter; the scarred area was surrounded by a substantial thickness of ventricular wall. Located subendocardially there was a well-demarcated circumferential rim of purple, soft myocardium occupying one-third of the thickness of the ventricular wall. The papillary muscles of the left ventricle showed similar changes. The subendoocardial rim involved the left half of the interventricular septum while the right half remained normal. The upper portion of the muscular septum in the region of the fibrous septum showed no evidence of infarction. Microscopy confirmed the macroscopic impression of a healed posterior myocardial infarction and a recent subendocardial infarction (of eighteen hours' duration) (fig. 4, C).

Except for the absence of deep Q waves in Leads II, III, and aVF, this patient showed the typical changes of posterior myocardial infarction. It is felt that most tracings of this type would be associated with acute posterior infarction but the possibility of subendocardial infarction must be considered. It is also felt that the scarring noted in the posterior wall was electrically silent and that the pronounced electrocardiographic changes noted were all due to the acute insult. This is the only case in this series in which subendocardial infarction resulted from acute thrombotic occlusion of one of the major coronary trunks. In view of the old occlusion of the right posterior descending branch, it seems possible that the left coronary artery carried the main or preponderant blood
A, Tracings show depressed RS-T segment in Lead I and elevated RS-T segments in Leads II and III, with monophasic action curve; depressed RS-T segments in the precordial leads and in Lead aVL with elevated RS-T segment in aVF. In spite of the absence of a prominent Q wave in aVF, the diagnosis was acute posterior infarction. B, Transverse section of the heart near the atrioventricular sulcus showing old posterior infarct and recent subendocardial infarct most pronounced posteriorly. There was an old recanalized thrombus in the right posterior descending coronary artery and a fresh thrombotic occlusion of the left anterior descending coronary artery. (1, Left ventricle; 2, right ventricle; 3, anterior; 4, posterior; 5, infarcted zone; 6, infarcted posterior papillary muscle.) C, Low-power photomicrograph showing scattered foci of fibrosis and subendocardial zone of acute infarction. (1, Epicardium; 2, endocardium; 3, zone of infarction.)
supply to the myocardium. Therefore, at the time of fresh occlusion of the left anterior descending coronary artery, the situation was tantamount to global impairment of the blood supply of the heart. However, this must remain a theoretic possibility only, for we have not the precise information regarding the coronary blood supply that would be provided by use of the technic of Schlesinger and Blumgart.11

Case 5. (P.B.B.H., 8A469). J.P., a 70 year old white man with hypertension and angina pectoris, was admitted to the hospital on June 28, 1948, because of an attack of acute myocardial infarction. On admission he was in shock with a blood pressure of 82/61. The electrocardiogram (fig. 5, A) showed an abnormal form of the ventricular complex with depression of the RS-T segments in Leads I and II, elevation of the RS-T segment in Lead III, and a biphasic T wave in Lead I with late inversion of the T waves in Leads II and III. The unipolar limb leads showed elevation of the RS-T segment in Lead aVR, depression of the RS-T segment in aVL, and upward bowing with late inversion of the T wave in aVF; there was no significant Q wave in aVL or aVF. The unipolar chest leads showed marked elevation of the RS-T segments in V1 to V6, tall R waves, depressed RS-T segments, and inverted T waves in V3 to V6. These changes were interpreted as characteristic of left ventricular hypertrophy and in addition as showing changes very suspicious of myocardial infarction of uncertain location, possibly transseptal (Roesler-Dressler) or subendocardial. The patient expired sixteen hours after the onset of the attack.

Autopsy showed cardiac enlargement (the heart weighed 600 grams) and coronary artery sclerosis without occlusion. Section of the heart (fig. 5, B) revealed a circumferential pale zone of myocardium 0.4 cm. in thickness beneath the endocardium studded with minute soft foci dark red and black in color. This zone became transmural at no point. Microscopic examination (fig. 5, C) showed this circumferential zone to be freshly infarcted (approximately sixteen hours' duration). When the gross sections of the heart were fixed it was noted that the borders of the infarct were serrated rather than linear; this was confirmed microscopically.

In reviewing the electrocardiograms in this case it might be conjectured that the standard and unipolar extremity leads showed a composite effect of posteroseptal or subendocardial infarction and left ventricular hypertrophy. Thus, whereas the RS-T segments in Leads I and aVL were depressed, the T wave in these leads was biphasic (minus-plus) rather than inverted, and the T wave in Lead III was biphasic (plus-minus) rather than upright. However, since tracing of this sort may be seen in uncomplicated left ventricular hypertrophy, a definite statement in this regard is not warranted.

Case 6. (P.B.B.H., 7A55). H.G., a 65 year old business man, with angina pectoris and hypertension, was admitted to the hospital on October 26, 1947, for excision of carcinoma of the rectum. The electrocardiogram (fig. 6, A) made one day after admission showed an abnormal form of the ventricular complex with depression of the RS-T segments in Leads I and II, biphasic T waves in Leads I and II, and deep QS waves in Lead III. The axis deviation index was plus 21 indicating an abnormal left-axis deviation. The unipolar limb leads showed a small Q wave, an embryonic R wave, a small S wave, and an R' approximately equal to S in Lead aVr but the total voltage was small in this lead. Unipolar chest leads showed elevation of the RS-T segments in Leads V1 to V6, and depressed RS-T segments with biphasic T waves in Leads V1 and V6. These tracings were interpreted as characteristic of left ventricular hypertrophy.

Surgery was carried out on the seventh hospital day. During the procedure the blood pressure dropped despite various therapeutic measures, and never returned to its preoperative level, and the urinary output was low. On the second postoperative day, the patient complained of distress in the epigastrium and a pericardial friction rub was heard. Profound changes now appeared in the electrocardiogram (fig. 6, B). There was a depression of the RS-T segments in Leads I, II, and III, maximal in Lead II. The RS-T segment in Lead aVR was depressed but a Q wave was present in neither aVL or aVF. The unipolar chest leads showed a late insinuoid deflection (R') in V1 and V6; a depressed RS-T segment in V1 to V6; maximal in V5 to V6; biphasic T waves in V5 to V6, and inverted T waves in V5 and V6. This tracing was regarded as very suggestive of subendocardial infarction of the anterior wall of the left ventricle.

The patient continued to do poorly. On the following day an electrocardiogram was made but owing to technical difficulties only Leads I and II were recorded. However, as incomplete as the study was, there was adequate electrocardiographic evidence to suggest posterior transmural infarction, for Lead II now showed a small Q wave and elevated RS-T segment (fig. 6, C). Later that day the patient went into profound shock, had a convulsion, and died.

The postmortem examination showed the heart to be enlarged, weighing 610 grams, with a left ventricular thickness of 2.5 centimeters. The infarction involved the subendocardial aspect of the
FIG. 5.—Subendocardial Infarction and Left Ventricular Hypertrophy (Case 5).

A. Tracings show depression of RS-T segments and biphasic T wave in Lead I; elevated RS-T segment in Lead III; elevated RS-T segment in aVR; depressed RS-T segment in aVL; elevated RS-T segment in V1 to V4; tall R waves in unipolar chest leads; depressed RS-T segments and inverted T waves in V5 and V6; no prominent Q wave in Lead III or Lead aVF. Tracings are characteristic of left ventricular hypertrophy and seem suspicious of superimposed myocardial infarction. B. Transverse sections through upper and lower halves of the heart showing thick left ventricle and circumferential purple subendocardial zone of infarction with serrated margins. (1, Left ventricle; 2, right ventricle; 3, anterior; 4, posterior; 5, infarcted zone.) C, Low-power photomicrograph showing intermingling of fibrotic (pale) and infarcted (dark) foci beneath the endocardium. (1, Epicardium; 2, endocardium; 3, infarcted zone.)
anterior, lateral, and septal (left side) portions of the left ventricle and was transmural in the posterior wall of the left ventricle. Microscopic examination showed a recent myocardial infarction. There was also a fibrous scar on the anterior wall of the right ventricle near the interventricular septum measuring 1.5 by 3.5 cm.; some scarring was also evident in the middle portion of the interventricular septum.

The coronary arteries showed severe arteriosclerosis but no total occlusion, thrombosis, or subintimal hemorrhage.

This case is of interest because, like some described by Pardee and Goldenberg and by Alzamora, the infarction apparently began as a subendocardial process, then became trans-

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**Fig. 6—Acute Subendocardial Infarction as a Prelude to Transmural Posterior Infarction (Case 6).**

A. Preoperative tracing is characteristic of left ventricular hypertrophy and shows notched QRS wave in aVF predominantly below the isoelectric line.

B. Tracing made the second day following operation. The hypotension persisted postoperatively. There is now depression of the RS-T segments in Leads II, III, and aVr; elevation of the RS-T segment in Lead aVr with late inversion of the T wave; striking depression of RS-T segments in V2 through V4; no Q wave in Lead III or aVr. These tracings were regarded as very suggestive of subendocardial infarction with incomplete right bundle branch block.

C. Leads I and II only, made on the third postoperative day. There are now a small Q wave and elevated RS–T segment in Lead II which were considered as evidence of acute posterior myocardial infarction. Postmortem examination showed a fresh infarct which was subendocardial on the lateral, anterior, and septal aspects of the left ventricle, transmural on its posterior aspect.
mural, and also in that the occasion under which it developed was postoperative hypotension.

**Discussion**

In an electrocardiographic-pathologic correlation of this sort it is important to bear certain facts in mind. First, the physicochemical phenomenon need not have reached the stage of an anatomic lesion before its electrical effects have become apparent. The functional disturbances which produced the electrocardiographic phenomena may thus have been much more extensive than the structural changes seen at autopsy. Therefore, one would not expect the distribution of the latter to correspond exactly with that of the former. Secondly, by choosing those cases (all but the last—Case 8, to follow) with a fatal issue, it is possible that a more serious prognosis has been attributed to the electrocardiographic changes observed than they necessarily warrant. Finally, in the natural electrocardiographic sequence of transmural infarction, displacement of the RS–T segment may precede the inception of QRS changes. Often the latter do not develop until the former have regressed. Experience has shown that a diagnosis of myocardial infarction is not warranted on purely electrocardiographic grounds unless both QRS and RS–T changes are recorded. In the presence of adequate supporting clinical evidence the diagnosis may be made on the basis of changes in the RS–T segment alone. The failure of QRS changes to appear early in the course of a clinical episode may then be due to the fact that infarction is not present, that infarction is limited to the subendocardium, or that evidence of transmural infarction has not yet developed but will with the passage of time. Indeed, the patient may die before these changes have become apparent. However, the persistent absence of QRS changes over a prolonged period in the face of RS–T displacement and corroborative clinical evidence of infarction would be more suggestive of a process limited to the subendocardium. The most striking feature of the tracings recorded in the present series, therefore, is the absence of characteristic signs of infarction. With the possible exception of figure 6, C (taken from the only individual who developed transmural infarction) none of the records would justify the diagnosis of infarction on the basis of the electrocardiographic changes alone. But in each case the electrocardiographic findings in conjunction with the clinical picture might justify the suspicion of subendocardial infarction.

A fair number of reports of cases with myocardial damage limited to or predominating in the subendocardial layers of the heart have already appeared in the literature. Bayley’s case showed myocardial necrosis more extensive at the subendocardial surfaces and apex than at the epicardial surfaces of the ventricular muscul. The electrocardiograms in this case showed the so-called “injury against the rule,” that is, displacement of the RS–T segments which are the reverse of those which occur in acute pericarditis. The first of 2 cases of myocardial infarction reported by Langendorf and Kovitz showed predominantly, and the second apparently exclusively, subendocardial involvement. Rather atypical bipolar (Leads I to III and CF₃, CF₁, and CF₅) electrocardiograms were recorded in these cases but RS–T depression over the left precordium was not described. The case of Price and Janes with tracings (Leads I to III and IVR) ascribable to posterior or posterolateral myocardial infarction, showed extensive subendocardial infarction. This was the first case in which the correspondence of the myocardial damage to a specific muscle bundle was suggested. The muscle corresponding to the subendocardial fibers of the superficial bulbospiral muscul was involved in this case.

Wilson and his co-workers showed that in myocardial infarction in man, as well as in experimental infarction in dogs, the endocardial aspect of the infarct is almost always larger than the subepicardial aspect. In many of their canine experiments the infarct did not penetrate the ventricular wall or was transmural over only a small area. When the infarct was transmural, deep QS waves were recorded. Where the infarct was subendocardial, as at the margins of a transmural infarct, there were abnormally large Q waves followed by subnormal R waves in the direct leads. There is no reason, therefore, why subendocardial infarcts
should fail to produce QRS changes. Since none were found in any case in the present series it would seem that these cases do not represent subendocardial infarction in general, but subendocardial infarction of a special kind.

Wilson and his associates have also demonstrated that an electrode overlying the epicardial surface of a fresh transmural infarct records an upward displacement of the RS–T segment at the same time that an electrode overlying the ventricular wall opposite this lesion records a downward displacement. Several other physiologic investigations have been concerned with the electrical effects of injury to the endocardium or subendocardial layers of the myocardium, particularly as concerns displacement of the RS–T segments. The gist of these studies is that injury confined to the subendocardial layers produces RS–T elevation in leads from the adjacent ventricular cavity as well as in leads from the epicardial aspect of the opposite ventricular wall, while RS–T depression is noted when the exploring electrode is over the epicardial aspect of the affected ventricular wall.

These studies point out the desirability, in evaluating the question of subendocardial infarction, of determining cavity as well as surface potentials. Cavity electrograms obtained by catheterization of the cardiac chambers in the experimental animal can give this information, but this is out of the question with human subjects suspected of myocardial infarction. It is here that unipolar extremity electrocardiography is most helpful. By virtue of the relatively fixed position of the base of the heart, the ring of the auriculoventricular valve faces the right shoulder. As a result, cavity potentials are transmitted through this ring to the right shoulder and the study of right-shoulder potentials (V_R or aV_R) gives virtually the same information as does a catheter electrode within the ventricular chamber. If the heart is in the vertical position electrically, the left shoulder (V_L or aV_L) may also reflect cavity potentials. A slight degree of elevation of the RS–T segment in Lead aV_R may be within normal limits. In 4 of the 6 cases of subendocardial infarction here recorded, however, aV_R showed a rather pronounced degree of upward displacement of the RS–T segment consistent with orientation of the injured area toward the ventricular cavity.

Pruitt and Valencia commented on the difficulty of producing subendocardial damage of sufficient extent and severity to produce measurable electrical effects while still sparing a zone of uninjured myocardium between the traumatized tissue and the epicardium. Nature, it seems, can fulfill the conditions of this experiment much more readily than can the physiologist. This has been explained as the result of the fact that the heart consists not of an homogenous mass of muscle but of an intricate system of interlacing muscle bundles with a spiraling, whorled arrangement. The disposition of these muscle bundles has been described by Mall, Robb, and Lowe and Wartman. Without describing in detail the origin, insertion, and course of these muscle bundles, and neglecting the muscle bundles which make up the right ventricle, it may be stated that the superficial sinospiral muscle constitutes roughly the subendocardial few millimeters as well as the subepicardial few millimeters of the anterior half or so of the left ventricle, while the superficial bulbospiral muscle has a roughly similar distribution posteriorly. Both of these, the superficial sino- and bulbospiral bundles, make up the entire thickness of the apical one-fourth of the left ventricle. The greater bulk of the muscle mass of the basalar three-fourths of the left ventricle lying between the subendocardial and subepicardial distribution of these superficial muscles is made up of three muscles—the deep bulbospiral, deep sinospiral, and the scroll muscle. These bundles have each their own blood supply. Lowe has demonstrated how injury can selectively involve specific muscle bundles. He felt that the cylindric scars sometimes seen in the ventricular walls may be due to obstruction of one of these small coronary branches. However, no reported case of subendocardial infarction in the small arteries was described nor were thrombi found in any of the smaller vessels in this series. Furthermore, since the parent artery gives branches to both the subendocardial and subepicardial portions of the superficial muscles, one would expect to find descriptions of simultaneous
infarction or scarring of the subepicardial and subendocardial shells. It seems, therefore, that some factor other than vessel obstruction is generally responsible for the necrosis of the subendocardial muscle bundles. Recent publications have tended to stress another aspect of the blood supply to the deeper muscle bundles. It has been pointed out, for example, that the blood supply to the left ventricle is derived from main coronary arteries which course down the epicardial aspect of the ventricles, giving rise to perforating branches at right angles to the main artery, and that these reach well into the subendocardium where there are apparently diffuse anastomotic channels. A gradient of pressure existing at the height of systole between the more superficial and deep layers of the ventricular wall has been demonstrated. Except for possible nourishment directly from the left ventricular chamber or via the thebesian channels, or through collateral subendocardial anastomoses, the subendocardium, being that part of the myocardium farthest removed from its blood supply, is the most vulnerable to partial or complete deprivation of its blood supply. It would, therefore, be in these remote parts of the heart that global (shock, anemia, syphilitic ostial disease, and like affections) rather than zonal restriction of coronary flow might be manifest.

The common denominator in all of our cases and in the few described in the literature was found to be a deficient irrigation, not of a single coronary artery, but of the entire coronary system, be it due to clamping down on coronary flow at its source by syphilitic ostial disease, to shock however produced, or to any condition producing systemic hypotension and consequent diminution of coronary blood flow. The occurrence of single or multiple coronary occlusions has been described under such circumstances by Blumgart, Schlesinger, and Zoll but in their cases a subendocardial distribution was not noted. The cases described above, then, are of the kind in which all, or almost all, of the subendocardial muscle becomes ischemic or infarcted as a result of a general disturbance of the systemic (shock) or of the coronary circulation. Under these circumstances it would seem that the forces produced in one part of the ventricular muscle may be cancelled by the effects produced in another. A uniform ischemia of all the subendocardial muscle would be expected to produce downward RS–T displacement in all of the usual leads except aVR, but it could hardly produce Q waves even after RS–T displacement had disappeared, for there would be nothing to make the ventricular cavities negative. As a matter of fact, if all of the subendocardial muscle failed to respond, the ventricle could not be activated. It must be supposed that the affected muscle did respond but responded abnormally (with a reduced change in the voltage across the membrane) or that the involvement of the subendocardial muscle was extensive but spotty.

This concept of coronary insufficiency was first developed by Büchner. He was well aware of the RS–T depressions developing in the precordial leads in some of the cases and of the subendocardial distribution of the resulting ischemia or infarction. This aspect of the concept was elaborated by Master and the role of the collateral circulation by Blumgart and his colleagues.

It is possible that study of the muscle bundle distribution may explain a rather curious finding in the pediatric literature. This is the so-called thickened endocardium which has been reported with or without hypertrophy of the heart in children, and has been attributed in some cases to a previous endocarditis. Some of the cases, however, lacked any evidence of inflammatory reaction. In light of the more recent anatomic studies, it is suggested that the apparent thickening of the endocardium may actually be due to fibrosis of the superficial sino- or bulbospiral muscles. In one such case the left anterior descending coronary artery was narrowed and among other possibilities it was suggested that the change may conceivably have been due to the consequent coronary insufficiency. Future studies of this condition should include a careful examination of the blood supply to the heart.

Alzamora felt that subendocardial infarction was a relatively benign process and that perhaps in only a very few subjects is the condition found at necropsy. That this is not necessarily true is suggested by the present study.
in which in 6 of 63 cases of fatal myocardial infarction a subendocardial distribution of the process was shown. It is our impression that these cases represent a type of myocardial infarction of particular distribution and arising under particular circumstances, but nonetheless with similar pathologic physiology and the same uncertain prognosis of the entire group.

Are based certain functional tests for that condition. Their inception and reversibility during other disturbances is also quite familiar. The electrocardiographic tracings shown in figure 7, A are those of a 64 year old woman with hypertensive heart disease and angina pectoris who developed auricular fibrillation during a stormy postoperative course following cholecys-

**Fig. 7.—Case 7**

*A.* Tracings made during a paroxysm of auricular fibrillation showing depressed RS-T segments in V₁ through V₃ and to lesser extent in V₁, V₂, and V₄; slight elevation of RS-T segment in aVR.

*B.* Curves showing reversion to normal rhythm brought about by quinidine therapy. Note disappearance of RS-T deviations. The first set of tracings resemble those occurring with subendocardial infarction, but the changes were reversible and possibly attributable to ischemia. Autopsy showed coronary sclerosis but no infarction.

Of myocardial infarction. It seems to us that to designate these merely as cases of coronary insufficiency is to minimize their gravity.

Under certain circumstances the described electrocardiographic changes need not indicate subendocardial infarction. Their occurrence as a transient phenomenon following or during spontaneous or induced angina pectoris has been well established and is the criterion upon which tectomy. The ventricular rate during the attack of abnormal rhythm was 164. At this time pronounced RS-T depression was noted in Leads I, II, aV₃R, and V₁ to V₆ and RS-T elevation in Lead aV₃R—changes of the same order as those described above. On reversion to normal rhythm (Fig. 7, B) following quinidine therapy the rate slowed to 56 and the RS-T segment displacements returned to the isoelec-
tric level. This patient's death was due to surgical complications. At autopsy some coronary sclerosis was noted but no subendocardial infarction. Electrocardiographic tracings shown in figure 8, A were obtained from a 59 year old housewife during a paroxysm of auricular tachycardia which had lasted about twenty-four hours. The RS-T displacements here noted line is quite striking. Generally, as in the examples cited, the reason for the changes will be quite obvious, be it angina pectoris or paroxysmal rapid heart action. Their development and persistence during an episode suggestive of acute myocardial infarction would be much more suggestive of actual infarction in the subendocardium.

FIG. 8.—Case 8

A. Tracings made during paroxysm of auricular tachycardia showing RS-T depression in V1 through V4; most pronounced in V2 through V4; slight elevation of RS-T segment in aVR.

B. Tracings made immediately following restitution of normal rhythm showing return of RS-T deviations to the isoelectric line. Because of their reversibility, the changes recorded in A may be attributable to subendocardial ischemia rather than infarction.

are quite commonly seen during such attacks, especially those of considerable duration. These changes are quite the opposite of those recorded in simple physiologic tachycardias where the rapid rate is apt rather to produce an elevation of the RS-T segment.28 Figure 8, B represents tracings made of the same patient immediately following reversion to normal rhythm with right ocular pressure. The prompt return of the RS-T segment to the isoelectric line is possible that the frequency of this finding in the present series may result, in large part, from our interest in the condition. We feel that if the electrocardiographer is alert to the type of tracing inscribed in this condition he will detect or suspect more cases of myocardial infarction limited to or predominant in the subendocardial layers of the myocardium, and that he will find many cases in which the process begins as a subendocardial
one and subsequently develops the characteristic electrocardiographic stigmas of transmural infarction. Meticulous pathologic examination may confirm this subendocardial distribution in a larger proportion of cases than hitherto reported.

**Summary**

Six instances of subendocardial myocardial infarction were encountered at autopsy among 65 cases of myocardial infarction. In 3 instances, the diagnosis was made or strongly suspected on electrocardiographic grounds. In a fourth case this possibility was entertained but acute cor pulmonale was considered more likely. In the fifth case the electrocardiogram was characteristic of left ventricular hypertrophy and in the last, suggestive of acute posterior myocardial infarction. The electrocardiographic clue to this condition was depression of the RS-T segment over the precordium, elevation of the RS-T segment in Lead aVR and the absence of a prominent Q wave in aVF, findings which, of themselves, do not justify the diagnosis of infarction, but which in conjunction with the clinical picture may herald transmural infarction or suggest subendocardial infarction.

In three instances there was extensive coronary arteriosclerosis without occlusion. In one, the left anterior descending coronary artery was occluded by a fresh thrombus but in view of a previous old occlusion of the right posterior descending coronary artery, the former vessel probably carried the greater part, if not all, of the blood to the left ventricle. In the second (Case 5), the arteriosclerosis was associated with syphilitic narrowing of the coronary ostia. In the third (Case 6), it followed postoperative shock. This last case was the only one in this series in which the subendocardial infarction was the prelude to a transmural infarction. In all of the cases, the infarction was limited to a rim of myocardium, usually circumferential, and distributed subendocardially with a tendency to involve the papillary muscles. Thrombi were not seen in the smaller coronary vessels in the neighborhood of infarction. The remarkable clinical feature of this group of cases was the uniform presence of shock. The facts presented here are consistent with the concept that the electrocardiographic and pathologic features of subendocardial infarction develop characteristically in conditions associated with impairment of the total coronary blood supply.

**Addendum**

We have reviewed the comprehensive and thorough studies of Gordon Myers and his colleagues since the present paper was submitted for publication. These observers found numerous instances of subendocardial infarction either localized to certain segments of the left ventricle (antero-septal, antero-lateral, lateral, septal, etc.) or, like those reported here, circumferential and involving all or most of the subendocardium; these were found in various stages of development from acute through organizing to healed. Old scars which were purely subendocardial or which were subendocardial extensions of transmural infarcts were generally correlated with QR deflections but, curiously, at times with QS deflections. In some cases QR complexes in Lead aVF (Goldberger) were noted in association with posterior subendocardial infarction. Acute or subacute subendocardial infarcts might be associated with depressed, isoelectric or elevated RS-T segments. Case 14 of their study showed pathologic changes such as those described in the present paper and, though the RS-T segment in Leads I and II was depressed, the electrocardiographic sequence consisted of the appearance and subsidence of changes of acute antero-septal infarction. Case 38 resembles the acute subendocardial infarcts described here in all respects. In case 146, although the electrocardiographic tracings resemble those described here, postmortem examination showed a transmural lateral infarct with anterior subendocardial “ischemia” only. These workers gave a number of explanations for the puzzling failure of Q waves to develop in acute subendocardial infarction. It seems to us that this is linked up with the extent of the subendocardial infarct. As a result of the extensive infarction of the entire subendocardial rim, no important area of the wall opposite the recording electrode is able to get a “heart start” in being activated; hence a Q wave does not
develop at the recording electrode. Electrically inconspicuous but adequate islands of intact myocardium are interspersed with the infarcted areas and transmit the activating impulse to the relatively healthy subepicardial layers. Yet the injured area is formidable enough to present a large “current of injury” oriented toward the endocardial aspect of the ventricle; therefore, RS-T segment depressions develop over the left ventricle and RS-T elevation at lead aVR.

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