Subendocardial infarction in retrospect: pathologic, cardiographic, and ancillary features

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ABSTRACT Fifty-three patients with subendocardial infarction (SEMI) were studied at autopsy; all were elderly and the group was equally divided by sex. About half had more than one SEMI: the recurrences or extensions often involved superjacent, but not infrequently adjacent, areas. Six showed fibrinous pericarditis. This larger study showed more widespread and severe coronary narrowing than an earlier report. Six patients had thrombi in the right coronary artery. Six showed electrocardiographic evidence of concomitant anteroseptal and inferior (Roesler-Dressler) infarction, and 12 had intraventricular block generally preceding higher-grade block or arrhythmias. At some time during their terminal hospitalization, 27 patients, or half, developed distinctive protracted RS-T depression or T wave inversion. Twenty-four of the SEMIs were diagnosed on accepted criteria as transmural infarct; that diagnosis was sustained in only four. Thus neither the presence of changes in RS-T segment or T wave nor the absence of QRS changes are mandatory for the diagnosis of SEMI; this invalidates the common assumption that the diagnosis is not justified unless these conditions are met.

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ON THE PRESUMPTION that it is uncommon\(^1\) relative benign,\(^3\),\(^4\) and represented in the electrocardiogram (ECG) only by changes in ventricular repolarization, subendocardial infarction (SEMI) was at first regarded as quite distinct from “garden variety” transmural infarction. Recent consensus, by contrast, has recognized SEMI as more common,\(^5\)–\(^9\) more serious in impact,\(^10\)–\(^13\) tending to recur or extend,\(^5\)–\(^9\),\(^14\)–\(^17\) and associated with changes in depolarization.\(^5\)–\(^9\),\(^16\)–\(^22\) By and large the diagnosis has been clinical and electrocardiographic and based on (1) a history of prolonged chest pain or compression, (2) the observation of a diagnostic rise in the peak level of enzymes in the blood, (3) the new development of widespread depression of RS-T segments (figure 1) or inversion of T waves (figure 2) lasting at least 48 hr, and (4) the absence of changes in the QRS complex. It has been assumed that satisfaction of these criteria establishes the diagnosis with the implication that, if the criteria are not met, the diagnosis is not justified.

Pathologic substantiation of the diagnosis has, to no small extent, been scanty or lacking. Confusion has been compounded by (1) inconsistent definition of the necessary extent of infarction, (2) the introduction of a less restrictive term, “non-transmural” myocardial infarction, which by some authorities is and by others is not used interchangeably with SEMI, (3) the more recent designations “Q wave” vs “non-Q wave” infarctions, and (4) the introduction into chemical parlance of such terms as “acute coronary insufficiency,” “unstable angina pectoris,” “rule out myocardial infarction,” “acute mild” or “acute atypical infarction,” and even the label SEMI itself, used with similar imprecision. Out of this overwhelming confusion and ambiguity emerges a compelling need for a wholesale reassessment of the entire subject, the point of departure being anatomic and the sole requirement for the diagnosis being the demonstration of bona fide SEMI at postmortem examination. Although subject to the distortion inherent in all retrospective studies, this offers the dividend of an incontestable verification of SEMI in every patient included.

Materials and methods

The clinical charts of 53 patients treated at Brigham and Women’s Hospital were reviewed and correlated with the autopsy findings of the same patients. Twenty-one of these were consecutive patients from a personal consultation practice (in this sense “selected”), and 32 were culled at random from autopsy records as they became available (thus “unselected”). All had indubitable (acute, healing, or healed) SEMIs and were accumulated over the years following an earlier publication from this hospital.\(^23\) Unless an anatomically distinct SEMI ex-

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FIGURE 1. Extreme RS-T shifts in an 81-year-old patient with acute SEMI (same patient as in figure 3). A. Tracings in 1978 showing normal sinus bradycardia (rate 50 beats/min) and tall R wave in V1 suggesting old posterobasal infarct. B. Tracings recorded on admission for acute chest pain showing atrial fibrillation, inconspicuous Q waves in leads II, III, and aVF, RS-T depression in leads II, III, aVF, and V2 to V6 with RS-T elevation in lead aVR. C. Tracings late that evening showing return to sinus bradycardia (rate 47 beats/min, sick sinus syndrome?) and persistent but less pronounced RS-T shifts. D. Preterminal tracings 2 days later showing sinus tachycardia (110 beats/min), more prominent Q waves in leads II, III, and aVF, and left bundle branch block.

FIGURE 2. T wave inversions during and after acute SEMIs. A. Tracings from 87-year-old man during initial hospitalization in 1970 for protracted chest pain and marked enzyme elevations, showing "localized" T wave inversion. B. Tracings on rehospitalization in 1974 for syncope and sustained interscapular pain with marked rise in creatine kinase level, showing sharp T wave inversion in leads V2 to V6, most pronounced in V3 and V4. C. Tracings 4 months later showing partial recession of T wave changes. D, ECG in terminal admission 2½ years later for lung abscess, showing left ventricular hypertrophy, prominent U waves, and atrial and ventricular premature beats. Postmortem examination showed lung abscess, atherosclerosis of surface coronary arteries, marked involvement of medium-sized arteries, two distinct subendocardial scars, but no acute infarct. Same patient as in figure 4.
There were 27 men and 26 women, the men averaging 69.1 years and the women 69.8 years at death.

Topography, age, and extent of SEMI. Almost half of the SEMIs were multiple. Of the 53 patients, 16 had single acute SEMIs (nine segmental, seven circumferential) (figures 3 and 4) and 13 had single old SEMIs (eight segmental, five circumferential). In 25 patients acute SEMI was associated with at least one healed SEMI considered to be separate from the acute infarct (figure 5); in 11 of the 25 there was more than one associated old SEMI. In a few of them repetitive SEMI had been recognized clinically (figure 6). In eight patients of the entire group the existence of old transmural infarction was also substantiated pathologically.

Most of the SEMIs were quite sharply layered (figure 3), many were irregular and mottled, a few were the obvious end-stage of a conglomeration of serial infarctions (figure 7), and one or two consisted of aggregations of similar but discrete punctate necroses. Although a deliberate numerical estimate of infarct depth was not attempted, general statements and color photographs indicated that most involved the inner third of the ventricular wall; in three it extended beyond two-thirds of the thickness of the ventricular wall. None extended to the epicardium.

Coronary artery stenosis in SEMI. The degree of stenosis of the LAD, measured in 30 patients, ranged from 50% to 100% (mean 90%, average 84.1%). Narrowing of the LCX, measured in 29, ranged from 40% to 100% (mean 85%, average 80%), and that of the RCA, measured in 38, ranged from 30% to 100% (mean 95%, average 90.1%), the latter including seven in whom the occlusion was total and partly or completely thrombotic (figures 4 and 11).

Papillary muscle dysfunction. Papillary muscle necrosis or fibrosis, generally of striking degree, was found in eight of the 53 patients. In all a well-marked systolic murmur had been heard before, or first developed during hospitalization of these 53 patients.

Study population. In the 36 patients in whom it could be estimated, the time from first SEMI to death ranged from 3 days to 15 years (mean 10 months, average 2.3 years). There were 27 men and 26 women, the men averaging 69.1 years and the women 69.8 years at death.

*Normal enzyme range at this laboratory (IU/liter): creatine kinase 50 to 60 (women), 50 to 180 (men); muscle band fraction of creatine kinase, < 2.2% of total creatine kinase; lactate dehydrogenase 88 to 196; and aspartate aminotransferase 22 to 47.
ing, the terminal hospitalization. In one patient the diagnosis was first suspected by the detection of this syndrome and the reflection that the papillary muscle may be considered an extension of the subendocardial laminae of the ventricular wall.

**Pericarditis in SEMI.** Paradoxically, six patients had clinical and pathologic evidence of acute pericarditis. In four a friction rub had been heard. Fibrous pericarditis was found in all six but in none did the infarct extend to the epicardium. In one, perivascular round cell infiltration was demonstrated in the pericardium. Rheumatoid arthritis or uremia may have been implicated in three but in the remaining three there was no explanation for the pericarditis other than SEMI.

**Mural thrombosis.** Left ventricular thrombi adjacent to SEMI were detected in only three patients, one with disseminated intravascular coagulation.

**Accessory noncoronary factors.** Search for factors ancillary to coronary arterial narrowing and adversely affecting myocardial oxygenation disclosed, in a substantial proportion of these patients, the six entities detailed in table 1 (see also figures 6 to 8).

**Cardiographic features.** Serial electrocardiographic tracings were available in 51 of the 53 patients. From the appearance of the tracings recorded initially in the terminal hospitalization, patients were divided empirically into five groups: (1) nine patients showing widespread depression of the RS-T segments persistent over at least 2 days, (2) seven patients showing widespread inversion of T waves also lasting at least 2 days, (3) 12 patients showing conduction disturbances.
Discussion

Pathologic aspects. For a population with coronary artery disease, this group was disproportionately elderly and female. That the degree of coronary narrowing in this expanded experience with SEMI exceeds that in the original handful of patients may be due simply to the selection bias of an aging population, but it poses the question of whether the elderly patient, and par-

FIGURE 6. Dynamic change of concurrent anterior and inferior (Roesler-Dressler) infarction recorded on 2 consecutive days in 1961 in a woman, then age 61, with angina pectoris and myxoedema of 10 years' duration. Subsequent acute infarcts occurred in 1962, 1966, 1968, 1975, and 1976, the latter two diagnosed clinically as subendocardial. "Cardiac scan" in 1977 was compatible with SEMI.

FIGURE 7. Same patient as in figure 6. Conglomerate old and acute SEMIs. The left main coronary artery was the site of an aneurysm extending to proximal left circumflex and left anterior descending arteries. The right coronary artery was totally occluded. All but one of the grafts had become occluded.

(atroventricular, intraventricular or fascicular block, and/or ventricular arrhythmias, (4) five patients regarded on the basis of currently and commonly employed criteria, including Q waves of significant duration, as having acute myocardial infarction, and (5) 19 patients regarded as having old myocardial infarction by similar criteria. Although serial tracings commonly continued to show the usual changes within each of these categories, many were unstable and evolved, as demonstrated in table 2, superimposed changes characteristic of one or more of the other groups.

TABLE 1
Factors ancillary to coronary narrowing affecting myocardial oxygenation

<table>
<thead>
<tr>
<th>General condition</th>
<th>n</th>
<th>Subgroups</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive blood loss or shock (or both)</td>
<td>5</td>
<td>Massive hemorrhage in ruptured AA</td>
<td>2</td>
</tr>
<tr>
<td>surgical or diagnostic procedures</td>
<td></td>
<td>Refused transfusion</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypotension after cardiac catheterisation</td>
<td>1</td>
</tr>
<tr>
<td>Myxoedema (figures 6 and 7)</td>
<td>4</td>
<td>Severe angina prevented</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>optimal control of hypothyroidism</td>
<td></td>
</tr>
<tr>
<td>Acute pulmonary embolism (figure 8)</td>
<td>8</td>
<td>Additional old SEMIs</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiple PEs</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SEMI preceded PE</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PE preceded SEMI</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sequence uncertain</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory collapse from other causes</td>
<td>2</td>
<td>Acute recurrent pneumothorax</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe cervical arthritis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>with acute spinal cord compression</td>
<td></td>
</tr>
<tr>
<td>Aortic valve disease</td>
<td>4</td>
<td>Significant aortic stenosis</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Significant aortic regurgitation</td>
<td>2</td>
</tr>
<tr>
<td>Abnormalities of blood</td>
<td>6</td>
<td>Blood dyscrasias</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pernicious anemia</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DiGuglielmo's leukemia</td>
<td>1</td>
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<tr>
<td></td>
<td></td>
<td>Sickle cell anemia</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DIC</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unusual chronic carbon</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>monoxide exposure</td>
<td></td>
</tr>
</tbody>
</table>

AA = aortic aneurysm; PE = pulmonary embolism; DIC = disseminated intravascular coagulation.
PATHOPHYSIOLOGY AND NATURAL HISTORY–SUBENDOCARDIAL INFARCTION

**TABLE 2**

Static and dynamic electrocardiographic features of SEMI

<table>
<thead>
<tr>
<th>ECG on admission</th>
<th>n</th>
<th>Early developments → Later developments</th>
<th>n</th>
<th>Pathologic highlights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protracted RS-T depression</td>
<td>9</td>
<td>IVB</td>
<td>2</td>
<td>Old TMI, acute anterior SEMI (fig. 11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Supraventricular tachycardia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Complete AVB</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No further ECG changes</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Protracted and widespread T wave inversion</td>
<td>7</td>
<td>Persistent T wave inversion</td>
<td>1</td>
<td>Diffuse disease of middle-sized coronary arteries, no acute infarct</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 yr → VF →</td>
<td>1</td>
<td>Acute segmental anteroseptal and lateral SEMI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No further ECG changes</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>LV</td>
<td>4</td>
<td>Higher grade IVB (figs. 9, 10)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>RBBB</td>
<td>6</td>
<td>Less pronounced IVB</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>LAH</td>
<td>2</td>
<td>VF</td>
<td>1</td>
<td>Old inferior TMI and acute circumferential SEMI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increasing AVB → acute anterolateral MI</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>→ acute inferior MI</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Acute TMI</td>
<td>5</td>
<td>IVB</td>
<td>2</td>
<td>(None of this group showed TMI)</td>
</tr>
<tr>
<td>Anterolateral</td>
<td></td>
<td>Increasing AVB (fig. 12)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Inferior RD infarct</td>
<td></td>
<td>RS-T elevation in inferior and anteroseptal areas</td>
<td>2</td>
<td>Old segmental SEMI and acute circumferential SEMI</td>
</tr>
<tr>
<td>Old TMI</td>
<td>19</td>
<td>RS-T depression in precordial leads</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pronounced T wave inversion</td>
<td>3</td>
<td>(Only 4 of this group showed TMI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bifascicular block with prolonged PR interval</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PVT → VF →</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute inferior MI</td>
<td>1</td>
<td>Acute circumferential SEMI and old MI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No further ECG changes</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

IVB = intraventricular block; AVB = atrioventricular block; LBBB = left bundle branch block; RBBB = right bundle branch block; LAH = left anterior hemiblock; TMI = transmural myocardial infarct; RD infarct = Roesler-Dressler infarct (ref. 27); PVT = paroxysmal ventricular tachycardia; VF = ventricular fibrillation.

particularly the elderly woman, is prone to infarction at the subendocardial level.

**Multiple infarctions and early recurrence.** From being subendocardial at their inception, myocardial infarcts, later in the same or in a subsequent acute episode, allegedly exhibit "transmural breakthrough."14, 28 Juxtaposition of scarred with freshly infarcted myocardium, as shown in figure 5, suggests rather that these were successive infarcts of different ages. The argument for successive infarction was supported in the present study by a frequent history of parallel and corroborative discrete repetitive clinical, enzymatic, and electrocardiographic episodes. From the multiplicity and the diverse location of SEMIs reported here, the contention seems valid that the conditions that led to the original SEMI may cause other areas, and not necessarily the superjacent subepicardium — the "new subendocardium" so to speak — to emerge as susceptible to infarction. This may explain Erhardt’s report9 that in 88% of his patients with terminal SEMI who had had previous infarcts, the earlier infarcts were also subendocardial, and the impression of Marmor et al.17 that each wave of necrosis may involve the same or a nearby site of coronary obstruction.

**Infarct size in SEMI.** The phenomenally high enzyme levels in patients with acute SEMI were quite unexpected. If peak enzyme level is correlated with the volume of infarcted muscle, these results suggest that SEMIs are large. Although thin compared with transmural infarctions SEMIs are more extensive and may wrap around a substantial portion, if not all, of the subendocardial circumference. Except in the study of
FIGURE 8. RS-T shifts attributable to SEMI and/or acute cor pulmonale. QRS changes attributed to transmural infarction. A. On admission, an 85-year-old woman with dyspnea and chest pain showed Q waves in leads III and aVF, depressed RS-T segment in leads I, aVL, and V₃ to V₆, elevated RS-T segment in aVR, and atrial and ventricular premature beats and was diagnosed as having acute inferior transmural infarction. B. Tracings on readmission 6 weeks later showing recurrent pain showing persistent Q waves in leads II, III, and aVF but much less pronounced RS-T shifts. C. Tracings after severe recurrence showed first-degree atrioventricular block and pronounced RS-T depression (“staircase ascent”) in leads I, aVL, and midprecordial leads and elevated RS-T in aVR. The patient then developed transient complete atrioventricular block and paroxysms of atrial flutter and fibrillation (not shown). Pulmonary embolism was suspected but ruled unlikely by lung scan. D. Terminal tracings showing persistent but less pronounced RS-T shifts, persistent P-R delay. Both acute pulmonary embolism and acute SEMI were found at postmortem examination.

Pericarditis in acute SEMI. Hutter et al.¹⁶ found pericarditis to be as frequent in nontransmural as in transmural infarctions. The finding of pericarditis in their study and in the present report is difficult to explain. The pericarditis of acute myocardial infarction is commonly considered to be caused by direct extension of infarction to pericardium and the detection of a friction rub decisive evidence for cross-the-wall infarction. Acute pericarditis may be the sole or predominant manifestation of Dressler’s postinfarction syndrome, which is commonly regarded as an autoimmune process. Many patients with pericarditis as a feature of that

FIGURE 9. T wave inversion and advancing conduction disturbances in a 91-year-old woman with acute myocardial infarction 1 year before SEMI. A. Tracings in initial hospitalization for painless congestive failure showing left anterior hemiblock and first-degree atrioventricular block with “poor R wave progression.” QRS complex was not prolonged. Peak creatine kinase level was 1224 IU/liter. B. Initial tracings in terminal admission 4 months later for severe dyspnea and chest pain, showing either intraventricular (possibly right bundle branch block with rightward and superior terminal forces) or “peri-infarction block” with left axis deviation of terminal 0.04 sec vector. Creatine kinase, 1500 IU/liter; MB fraction increased. C. Preterminal tracings the next day. The PR interval and QRS complex were still prolonged. RS-T depression and T wave inversion were more prominent in leads V₃ and V₆. Autopsy showed old healed circumferential and acute posterior segmental SEMI.
syndrome, blossoming sometime after an acute infarction, have in retrospect manifested that very same complication during their initial acute infarction. If the recurrence is autoimmune in nature, the same might be assumed for the original bout of pericarditis, a possibility considered but rejected by Hutter et al. If this argument is valid, these patients could appropriately be considered to have an accelerated or “syn-infarction” autoimmune pericarditis. In other words, the concomitance of pericarditis with infarction need not signal extension of infarct to pericardium. Unfortunately, although potentially pertinent, serologic or im-

![Figure 10](image1.png)

**FIGURE 10.** SEMI associated with bifascicular and possibly trifascicular block (right bundle branch block, left anterior hemiblock, and prolonged PR interval, best seen in lead V; the latter compatible with delayed conduction in atrioventricular conduction system or in posterior fascicle of left bundle branch). Alternative or additional anomalous atrioventricular excitation not excluded. This 84-year-old patient with tertiary lues and healed tuberculosis had periodic complete atrioventricular block in terminal admission. Autopsy showed healed posterolateral and apical SEMI, in some areas only recently healed.

![Figure 11](image2.png)

**FIGURE 11.** Left bundle branch block developing in patient with old inferior transmural infarct and fresh segmental SEMI. Serial tracings in terminal admission of 75-year-old hypertensive woman with previous angina pectoris. A, Tracings showing the R wave voltage and RS-T shifts of left ventricular hypertrophy. B, Tracings 2 days later suggesting old transmural infarction, still lacking left precordial Q waves but now with deeper and straighter RS-T depression in leads V; to V; a change that persisted for several days and measured 5 to 6 mm the day before death. C, Preterminal tracings showing complete left bundle branch block. Postmortem examination showed old inferior wall scar and acute “almost transmural” segmental anterior wall infarct. The left main coronary artery was more than 90% occluded, and the right coronary artery was the site of acute thrombus producing 90% stenosis of its lumen. Aortic stenosis was also present.
munologic data were not obtained in these patients.

Cardiographic aspects. At the onset of their terminal illness, nine patients showed protracted RS-T segment depression and seven had protracted and widespread T wave inversion. An additional 11 (e.g., figures 9 and 11) developed such changes during that hospitalization. Thus 27 showed changes in repolarization. Clearly, if we depend on RS-T or T wave changes for the diagnosis, it would have been missed in about half of these 53 patients. Furthermore, in none of the five patients diagnosed on the basis of QRS and T wave changes as having acute transmural infarction and in only four of 19 diagnosed on the basis of QRS changes as having old transmural infarction was coexistent transmural infarction substantiated at postmortem examination. These observations support the growing protest that in SEMI, the ECG may indeed show changes in, or even restricted to, the QRS complex and that it is erroneous to exclude that diagnosis if significant Q waves are recorded. Possibly pertinent are the observations of Wilson et al. that QS complexes may be recorded at an epicardial electrode overlying the transmural core of a full-thickness wedge-shaped infarct and QR complexes at the flanking epicardial surface tapping intact subepicardium overlying the subendocardial extension of such an infarct.

Are there other possible electrocardiographic clues to the diagnosis? The cluster of six patients developing changes attributable to concurrent inferior and anteroseptal infarction (Roesler-Dressler infarcts, figure 6) is noteworthy. Although Roesler and Dressler implied that these infarcts are primarily septal and that the anterior and inferior “transmural” portions are an extension of, and part and parcel of, the septal infarct, this electrocardiographic configuration may serve as a clue to a subendocardial location on the empiric ground of the present experience alone.

It is difficult to explain this type of infarct on the basis of current electrocardiographic teaching. One possibility is that the changes may be artifactual and the result a much faster spread of the activating impulse along the endocardium than its centrifugal conduction through working myocardium. Activation at the endocardial aspect of the anterior and posterior walls might then be only slightly out of phase and, assuming the direction of anterior activation to be about 180 degrees from that of posterior activation, the “anterior” and “inferior” R waves could in effect cancel each other, inducing QRS changes suggesting coexistent transmural infarction at both poles. Nor is the development of advancing intraventricular or atrioventricular block or of ectopic ventricular rhythms, as
observed in this study, distinctive of SEMI, attesting the subendocardial substructure of all myocardial infarcts. Perhaps the best that can be anticipated would be a differentiation between SEMI and transmural infarction based on statistical probability. The concepts underlying "peri-infarction block" and the "hemiblocks," proposed and developed during the past generation, must have a profound potential bearing on this diagnosis. During their terminal illness and before going on to higher-grade block or arrhythmias, 12 of these 53 patients developed either peri-infarction block (figure 9) or hemiblock (figure 10). Although Grant et al. and Rosenbaum et al. attributed these changes to conduction disturbances in the bundle branches, the latter emphasized that necrosis of heart muscle per se at or near the subendocardium may induce more profound electrocardiographic changes than similar damage near the epicardium. Certainly these "Roesler-Dressler" infarcts, as well as peri-infarction blocks and hemiblocks, deserve further study as possible indicators of SEMI.

The "head start" intrinsic to its gradual partial depolarization before end-diastole presumably explains the normal domination of Purkinje tissue over the cardiac rhythm. The frequency of block and ectopy in patients with SEMI may be explained by (1) the fact that electrical activation, which proceeds outward from endocardium to epicardium, is at the mercy of blood flow, which proceeds inward from epicardium to endocardium, and (2) the concentration of the major trunks of the atioventricular conduction system at the crest of the interventricular conduction system and the rich subendocardial distribution of the Purkinje network. The resultant propensity to ectopy may be enhanced by electrochemical changes at the margins of infarcted tissue and perhaps by a tactile vulnerability analogous to the induction of premature ventricular beats on simple contact of catheter tip with ventricular endocardium.

These findings may be discounted because this is a retrospective study, but they cannot be ignored. The court of final appeal remains the postmortem examination. A prospective approach is not disparaged; rather a modification in guidelines and in the direction of future studies, prospective or retrospective, is encouraged, including more frequent ventriculographic studies, data bearing upon an autoimmune state, a forthright statement of how many patients underwent autopsy, precise measurement of depth and volume of infarcted muscle, and explicit determination of whether, and over how large an area, the process of infarction actually reached the epicardium.

I am happy to express my sincerest gratitude to the late Dr. Monroe J. Schlesinger, who encouraged my continued interest in SEMI; to many colleagues at the Brigham and Women's Hospital, including Drs. Thomas W. Smith, Eugene Braunwald, Peter L. Friedman, Fred Schoen, Ramzi S. Cotran, and B. Leonard Holman, for their invaluable criticism of the manuscript; and through correspondence to Dr. Thomas E. Lowe of Toorak, Australia (regarding muscle bundles), Dr. Jesse E. Edwards of St. Paul (regarding semantics), Dr. Tom Raffin of Stanford, and Dr. Goodwill M. Stewart (who referred many of these patients to me in consultation). My heartfelt thanks also go to Mrs. Beatrice Scheff for invaluable secretarial assistance and to Barbara for a half century of constant support and forebearance.

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H D Levine

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