Clinicopathologic Correlations in Coronary Atherosclerosis
Four Hundred Thirty Patients Studied with Postmortem Coronary Angiography


Current progress in palliative surgery and in direct surgical approaches to the coronary arteries make detailed knowledge of coronary artery disease mandatory. Many investigations of coronary artery disease by different approaches have been reported, but the number of studies by injection technic are limited and have given rise to certain disagreements.

Merkel in 1906 first used radiopaque substances for injection of the coronary arteries post mortem. In 1938 Schlesinger devised his now classic method of injection of the coronary arteries, with which, in 1940, Blumgart, Schlesinger, and Davis carried out an extensive clinicopathologic study of angina pectoris, coronary thrombosis, and myocardial infarction. Although intercoronary arterial anastomoses have been recognized and studied for many years, the most comprehensive study of these anastomoses was made by Zoll, Wesseler, and Schlesinger in 1951, using the coronary injection technic and actual dissection in a series of over 1,200 human hearts. Recent studies by Snow et al and by Laurie and Woods have stimulated new interest in coronary anastomoses and their function. Moreover, some of these recent studies have taken exception to certain of the chief conclusions of Blumgart and his co-workers.

The present report is part of an extensive study of the clinical and pathologic features of coronary artery disease in the population of a general city hospital in the northeastern United States. Details of the extensive radiographic and pathologic data will be reported elsewhere; the present report considers primarily clinicopathologic correlations, with particular attention to the relationship of coronary occlusion to myocardial infarction, the incidence and importance of intercoronary anastomoses, the pathologic findings in angina pectoris, the accuracy of the clinical diagnosis of myocardial infarction, and finally the accuracy of the clinical assessment of coronary artery disease.

Materials and Methods

Selection of Cases

At the Mallory Institute of Pathology at the Boston City Hospital, from August 1957 to May 1959, a series of 430 hearts was studied by a modified Schlesinger-Reiner-Rodriguez coronary-injection technic, combined with a meticulous exploration of the coronary arteries and the myocardium. The hearts of the first three patients that died each day were selected for study as a representative sample of the autopsy population at this institution. It should be noted that medicolegal cases, cases with known active tuberculosis, and infants

From the Thorndike Memorial Laboratory and the Second and Fourth (Harvard) Medical Services, and the Mallory Institute of Pathology, Boston City Hospital, and the Departments of Medicine and Pathology, Harvard Medical School, Boston, Massachusetts.

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CORONARY ATHEROSCLEROSIS

were not included, and that, by chance, disproportionately few children were examined, none below age 13.

Injection Procedure

The coronary arteries of the hearts obtained at autopsy were injected simultaneously with a radiopaque mass consisting of barium sulfate in a menstruum of gelatin at room temperature. This mass remains confined to the arterial side of the circulation and can penetrate regularly to arterioles 40 to 50 μ in diameter. The menstruum injected into the right coronary artery was artificially colored red, and the menstruum injected into the left coronary artery was colored green. Because the capillaries and veins were uninjected, the primary distribution and ultimate terminations of the coronary arterial tree were delineated. A pneumatic apparatus, in which the pressure could be controlled accurately, was employed for injection. The injection pressure was gradually raised to 200 mm Hg, was maintained at that level for 5 minutes, and then the injection was terminated.

After injection of the radiopaque mass, the heart was “unrolled” to display the major coronary arteries in one plane. An angiogram was then taken, followed by a careful combined cross-sectional and longitudinal dissection of the coronary arteries. The findings were recorded on tracings made by superimpositions of the x-ray angiograms by transillumination. The ventricles were then sliced in coronal fashion, and a second set of radiograms was taken. The findings in the myocardium were recorded on tracings made from superimposition of the x-ray angiograms. Multiple sections were taken from representative sites of the ventricles, and in selected cases giant histologic sections of the whole ventricles were prepared. In the present study, a pathologic diagnosis of myocardial infarction was made if focal myocardial lesions greater than 5 mm, in their greatest cross section were found to be present.

The technic demonstrates (1) the anatomic pattern of the coronary arteries, (2) distortion or narrowing of the coronary arteries due to disease, (3) intercoronary arterial anastomoses greater than 40 μ, and (4) topographic relationships between sites of coronary narrowing and ischemic damage.

The technic will be reported more comprehensively elsewhere, where the limitations of interpretations of angiograms will be discussed in detail. The dissections were most valuable in revealing some coronary lesions not evident on the angiograms, and unmasking some filling defects as artifacts.

Grading of Atherosclerosis

For the purpose of the present study, coronary atherosclerosis was graded according to the maximum stenosis present in any of the main coronary arteries or the large branches, as judged both by dissection and by x-ray appearance. Number, length, or location of vascular segments involved was not considered. All cases were grouped as follows:

1. Mild stenosis—hearts without coronary narrowing or with narrowing resulting in reduction of the diameter of the lumen by 25 per cent or less.
2. Moderate stenosis—hearts with coronary narrowing reducing the diameter of the lumen by 26 to 50 per cent.
3. Severe stenosis—hearts with coronary narrowing reducing the diameter of the lumen by more than 50 per cent but short of occlusion.
4. Occlusion—complete occlusion of a major coronary artery or a primary branch.

Hearts were considered hypertrophied in males if they weighed 400 Gm. or more, and in females if they weighed 350 Gm. or more.

Interpretation of Clinical Records and Diagnostic Criteria

Independently, and without any autopsy data, the clinical records were reviewed in detail with special attention to all evidence of abnormal cardiac structure or function. In the first 250 cases all outpatient records and available summaries of admissions to other hospitals were studied. These were found not to contribute significantly to the final appraisal of the cases; in the final 180 cases only the inpatient hospital records at the Boston City Hospital were reviewed. The two groups of 250 and 180 cases did not differ clinically or pathologically in their over-all complexion.12 All available electrocardiograms were reviewed. Each patient was classified into one of four clinical categories with respect to the coronary circulation. Although classification was often difficult and at times arbitrary in this retrospective study, the usefulness of this system outweighed its limitations. The four categories are

1. Definite clinical coronary artery disease—patients with definite myocardial infarction, definite angina pectoris, or both.
2. Probable clinical coronary artery disease—patients with probable myocardial infarction, or possible although atypical angina pectoris.
3. Possible clinical coronary artery disease—patients with nonvalvular congestive heart failure, subacute or chronic, without angina or myocardial infarction, with or without hypertension, and patients with questionable myocardial infarction.
4. No clinical coronary artery disease—patients meeting none of the above criteria.

For the purpose of this classification, “valvular heart disease” was based on a clinical diagnosis only. Patients with this diagnosis were placed in
Table 1

Incidence of Clinical and Pathologic Characteristics in 130 Patients Grouped According to Severity of Coronary Artery Disease at Autopsy

<table>
<thead>
<tr>
<th>Pathologic classification of severity of disease</th>
<th>Composition of group</th>
<th>Classification</th>
<th>Clinical</th>
<th>Diagnosis</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Number (M:F)</td>
<td>Number (M:F)</td>
<td>Age (years)</td>
<td>Number (M:F)</td>
<td>Number (M:F)</td>
</tr>
<tr>
<td>+++</td>
<td>84 (45:39)</td>
<td>9 (14:20)</td>
<td>72.9 ± 9.6</td>
<td>9 (14:20)</td>
<td>9 (14:20)</td>
</tr>
<tr>
<td>++</td>
<td>113 (67:46)</td>
<td>6 (12:10)</td>
<td>71.3 ± 10.5</td>
<td>6 (12:10)</td>
<td>6 (12:10)</td>
</tr>
</tbody>
</table>

*Excluding valvular disease. Whenever the total number of patients differs from the reference group, the appropriate number is given in parentheses.

1. Tantalizing angina—subternal chest pain.
2. Typical angina—subternal chest pain, radiating to the arms, jaw, etc. A decrease in activity or emotion and not cleared by nitroglycerin.
3. Questionable acute myocardial infarction—good history, with or without suggestive electrocardiographic changes alone.
4. Definite acute myocardial infarction—good history, with supporting electrocardiographic changes alone.
5. Probable acute myocardial infarction—good history, with supporting electrocardiographic changes, or with sudden death before historical or laboratory evidence could be obtained in the absence of death. The electrocardiographic changes were not clearly described as to activity or emotion and not cleared by nitroglycerin.
6. Unspecified acute myocardial infarction—good history, with supporting electrocardiographic changes, or with sudden death before historical or laboratory evidence could be obtained in the absence of death. The electrocardiographic changes were not clearly described as to activity or emotion and not cleared by nitroglycerin.

ALLISON ET AL.
Figure 1
Incidence and distribution of coronary artery disease in 430 hearts examined by postmortem injection and dissection.

Congestive heart failure:
None, slight, moderate, or severe, according to the degree of symptoms and signs related in the record.

Results
Tables 1 and 2 summarize the data.

The Sample
The average age of the 430 patients studied was 68 years; the range was 13 to 96. There were 238 males (55 per cent) and 192 females (45 per cent); 374 whites (87 per cent), and 56 Negroes (13 per cent). Eleven of 430 patients, or 2.6 per cent, were of Jewish origin. There were two patients of Oriental origin, both Chinese.

The patients studied represent a broad sample of individuals dying in a large general city hospital in which most racial and ethnic groups of the northeastern United States are represented.
Table 3

Distribution of Coronary Artery Disease by Sex and by Decades

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Sex</th>
<th>Total number</th>
<th>Coronary artery disease</th>
<th>Myocardial infarction</th>
<th>Anastomoses</th>
<th>Angina pectoris</th>
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<tbody>
<tr>
<td>10-19</td>
<td>M</td>
<td>2</td>
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<td>0</td>
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<tr>
<td></td>
<td>F</td>
<td>1</td>
<td>1  0  0  0  0  0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>20-29</td>
<td>M</td>
<td>2</td>
<td>1  0  0  0  0  0</td>
<td>0</td>
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<td>F</td>
<td>1</td>
<td>1  0  0  0  0  0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>M</td>
<td>6</td>
<td>5  0  0  0  0  0</td>
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</tr>
<tr>
<td></td>
<td>F</td>
<td>6</td>
<td>2  0  0  0  0  0</td>
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<tr>
<td>40-49</td>
<td>M</td>
<td>12</td>
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</tr>
<tr>
<td></td>
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<td>50-59</td>
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<td></td>
<td>F</td>
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<td>14 0  0  0  0  0</td>
<td>8</td>
<td>16</td>
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<tr>
<td>60-69</td>
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<td>6  0  0  0  0  0</td>
<td>21</td>
<td>25</td>
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</tr>
<tr>
<td></td>
<td>F</td>
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<td>8</td>
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<tr>
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<td>26</td>
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<td></td>
<td>F</td>
<td>59</td>
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<td>15</td>
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<tr>
<td>80-89</td>
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<td>12</td>
<td>12</td>
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</tr>
<tr>
<td></td>
<td>F</td>
<td>49</td>
<td>1  0  0  0  0  0</td>
<td>22</td>
<td>7</td>
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</tr>
<tr>
<td>90-99</td>
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<td>1</td>
<td>0</td>
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</tr>
<tr>
<td></td>
<td>F</td>
<td>4</td>
<td>0  0  0  0  0  0</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Incidence and Distribution of Coronary Artery Disease

Coronary artery disease was present in 82 per cent of the hearts examined and was severe in 43 per cent (fig. 1). The gradations of severity, from none to occlusive, were of approximately equal incidence.

One or more occlusions of a major coronary artery or of a primary branch of a major coronary artery were present in 103 hearts (24 per cent), with a total of 227 occlusions. Forty occlusions were fresh and 187 were old. Forty-three hearts had one occlusion, 28 hearts had two occlusions, 32 hearts had three or more occlusions. The distribution of coronary artery disease in men and women by decades is shown in table 3.

In 1941, Schlesinger and Zoll,13 using a similar injection technique plus careful dissection, reported 94 hearts with occlusion in a series of 400 unselected hearts, an incidence of 23.5 per cent. They further compared their figures with earlier series of un.injected hearts and concluded that more than one half of points of occlusion in coronary arteries are overlooked by ordinary dissections. The present data are in agreement and point up the value of coronary injection plus careful dissection in determining the true incidence of occlusive disease at autopsy. Ravin and Geever14 in 1946 found occlusions in 18 of 166 injected hearts or 11 per cent. This lower incidence was most likely related to the younger age of their group.

Myocardial Infarction

One hundred and forty hearts (32.6 per cent) had one or more myocardial infarctions. The average age was 71.2 years (range from 35 to 96 years). The group included 82 men and 58 women, 126 whites and 14 Negroes. The infarcted group did not differ from the series as a whole in these aspects. The 140 infarcted hearts contained a total of 198 myocardial infarcts. Forty-seven were acute, 21 were healing, and 130 had healed. Fifty-two were considered small in size, 64 medium, and 82 large. A single infarct was found in 85 hearts (61 per cent), whereas 52 (37 per cent) had two infarcts, and only three (2 per cent) had three myocardial infarcts.

Intercoronary arterial anastomoses were found in 111 (79.3 per cent) hearts with myocardial infarcts. Cardiac hypertrophy was present in 102 (73 per cent). Thirty-seven
CORONARY ATHEROSCLEROSIS

(26.4 per cent) of the patients with myocardial infarctions had had angina pectoris, 48 had had chronic hypertension, and 11 had had hypertension for an unknown length of time. In 21 patients severe chronic congestive heart failure had been present; 54 had mild to moderate chronic congestive heart failure. Twenty of the cases with myocardial infarctions had valvular disease; aortic stenosis was the lesion in 13 of these. One hundred and two of the 103 hearts with coronary occlusions had myocardial infarction.

In 38 (27 per cent) of the hearts with myocardial infarction no coronary occlusion was present. All but one of these 38 hearts were affected by coronary artery disease, which was severe in 22 and mild to moderate in 15. In all 15 cases with mild to moderate coronary artery disease there were factors that may have contributed to the infarction: three had anemia, four had aortic stenosis, one had mitral stenosis with massive cardiac hypertrophy and severe chronic congestive heart failure, two had hypertensive heart disease with marked cardiac enlargement, two had diabetes, and three had severe pulmonary disease. The single heart with a myocardial infarct with no coronary artery disease was that of a patient with diabetes and chronic anemia. Hearts with and without occlusions are compared in table 4. The infarcts without occlusion were characterized as a group by being small, single, not accompanied by angina, and clinically not evident.

**Intercoronary Arterial Anastomoses**

In 140 of the total series of 430 hearts (32.6 per cent) intercoronary arterial anastomoses were demonstrated by the criteria and technic proposed by Schlesinger. In all but one of the hearts with coronary occlusion, intercoronary arterial anastomoses were present. The single exception was a heart with a single fresh occlusion in a primary branch of the left anterior descending artery with a corresponding fresh myocardial infarct. No other coronary artery disease was found in this heart.

By the technic indicated above, hearts with occlusions accounted for the majority of anastomoses found. Of the 76 hearts without coronary artery disease, only eight (10 per cent) had anastomoses.

In general, the data of the present study support the studies of Zoll, Wessler, and Schlesinger, who applied similar methods to a different sample in the same city.

Zoll and his associates also found that conditions other than coronary artery disease were associated with an increased incidence of intercoronary arterial anastomoses. These were anemia, cardiac hypertrophy, valvular heart disease, and cor pulmonale. They reported a 9-per cent incidence (9 of 101) of intercoronary anastomoses in the absence of coronary artery disease and thought that these other conditions stimulated the formation of intercoronary anastomoses. Our data differ in that anemia, cardiac hypertrophy, valvular heart disease, and cor pulmonale did not increase the incidence of intercoronary anastomoses, which was about 10 per cent in hearts having no coronary artery disease, regardless of anemia or hypertension.

The data reported by Laurie and Woods differ greatly from the results of the present study. These authors studied 150 Bantu hearts and reported "functionally significant" anastomoses in 75 per cent (31 of 41) of normal hearts of patients over 4 years of age, and in only 23 per cent (10 of 43) of

**Table 4**

<table>
<thead>
<tr>
<th>Clinical diagnosis of infarct</th>
<th>38 Cases without occlusion (per cent)</th>
<th>102 Cases with occlusion (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Medium</td>
<td>39</td>
<td>14</td>
</tr>
<tr>
<td>Large</td>
<td>45</td>
<td>32</td>
</tr>
<tr>
<td>Acute-healing</td>
<td>15</td>
<td>55</td>
</tr>
<tr>
<td>Healed</td>
<td>63</td>
<td>69</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>36</td>
<td>32</td>
</tr>
<tr>
<td>Size of infarct</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Age of infarct</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Multiple infarcts</td>
<td>62</td>
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</tbody>
</table>
hearts of patients with chronic ischemic heart disease. How can the difference be explained? Several possibilities exist. The present study deals with an older population with a higher incidence and a greater severity of coronary artery disease. Furthermore, Laurie and Woods failed to mention anemia, which is known to have a high incidence in the Bantu and is a known stimulus to intercoronary arterial anastomoses. Finally, the possibility exists that their injection technic, which perfuses one instead of two coronary ostia, permits demonstration of intercoronary anastomoses not evident with the technic used in the present study. This latter possibility is given support by a recent study of Reiner et al., who injected only one coronary artery and found an increased incidence of intercoronary artery anastomoses, as well as by unpublished data from this laboratory. As a subsequent communication will indicate, the incidence of anastomoses in the absence of coronary sclerosis may be a function of the injection technic used. By use of higher pressures for injection of the contrast media, and by injection of a single vessel or parts of one vessel at one time, a greatly increased incidence of anastomoses can be demonstrated in so-called "normal" hearts.

**Coronary Occlusion without Myocardial Infarction**

Of the 227 occlusions in our series, a total of 14 occlusions (6.2 per cent) in 11 cases did not result in myocardial infarction in relation to the vessel occluded. All 14 occlusions were primary, that is they did not develop distal to another occlusion. Three were in the right coronary artery, seven in a primary branch of the right coronary artery, one in the left anterior descending artery, and three in a primary branch of the left anterior descending artery. All had extensive intercoronary anastomoses tailored to fit the need for them. Ten of the 11 hearts, with 13 of the 14 occlusions, had additional myocardial infarctions with corresponding occlusions or narrowings elsewhere in the heart. The eleventh case was the only one in the entire series of 430 hearts that had an isolated occlusion in a heart completely free of grossly visible infarction.

The present data imply that pathophysiologically the coronary arteries act as end arteries; the vast majority of coronary occlusions are followed by myocardial infarctions. The data also indicate that coronary occlusion may occur without myocardial infarction, implying that intercoronary arterial anastomoses may afford complete protection from myocardial infarction. Such an occurrence is rare, however, and will be discussed in more detail in a subsequent report.

There has been some differences of opinion expressed in several published reports regarding the occurrence of complete coronary occlusion without myocardial infarction and the degree to which collateral vessels protect the myocardium from necrosis. A comparison of the present data with those of others is difficult because of differences in the methods of analyzing and reporting. Blumgart and his group in 1940, and others before them, presented evidence that coronary occlusion could occur without myocardial infarction. In that study of 125 consecutive autopsies, there were 27 hearts with occlusions. In 10 hearts with 25 old occlusions no infarcts were found. In 1946, Ravin and Geever in a series of 166 hearts encountered 18 hearts with one or more coronary occlusions. Five of these 18 hearts (28 per cent) with occlusions did not have myocardial infarcts. There were five additional cases in which infarction occurred only after multiple occlusions. The total number of occlusions was not stated in this paper. The authors stressed the relation between the development of anastomoses and the prognosis and treatment of coronary arteriosclerosis and occlusion. Snow and his group in Manchester, England, confirmed that myocardial damage caused by occlusion may be reduced by the development of a collateral circulation. They considered complete prevention of infarction uncommon because of 91 occlusions, only 13 (14 per cent) did not result in infarction. All of these had developed distal to pre-existing occlusions in arteries supplying previously infarcted areas.
Thus, although the incidence is lower than Blumgart’s, the occurrence of coronary artery occlusion without myocardial infarction is confirmed in the present study. But the fact remains that the majority of coronary occlusions are accompanied by myocardial infarctions.

**Angina Pectoris**

Typical angina pectoris had been present in 41 of 430 unselected cases, or in 9.5 per cent. In 1951, Zoll, Wessler, and Blumgart reported on 177 cases of angina pectoris in a series of 905 unselected autopsies at the Beth Israel Hospital, Boston, an incidence of 19.6 per cent, or twice that at the Boston City Hospital.

The present series of 41 patients with angina had an average age of 69.2 years (range 35 to 88), and comprised 21 men and 20 women, 33 whites and eight Negroes. In three of the 41, angina was of recent onset, i.e., less than 6 months’ duration, while in 38 it was considered chronic. Thirty-two of 41 patients (78 per cent) with angina had occlusive coronary artery disease: 24 of these had old occlusions, four had fresh occlusions, and four had both old and fresh occlusions. Myocardial infarcts were demonstrated in 37. Five had acute or healing myocardial infarctions, 15 had healed myocardial infarctions, and 17 had both acute-healing and healed infarctions. Intercoronary arterial anastomoses were present in 36 of the 41. Thirty-eight had suffered congestive heart failure, which was chronic in 32 and recent in six. There were two cases of aortic stenosis and one case of mitral stenosis in this group. In five of the nine cases of angina without coronary occlusion the cause was evident: they had severe coronary narrowing and myocardial infarction. The remaining four cases showed lesser degrees of coronary artery disease and had chronic congestive heart failure and cardiac hypertrophy; three had chronic anemia and three had hypertension. One had severe chronic pulmonary disease with cor pulmonale. The 32 patients with angina with occlusions represent only 31 per cent of all the patients with coronary occlusions, i.e., 32 of 103. The 28 patients with angina with old occlusions represent only 31 per cent of the 90 patients with old occlusions.

Patients with old coronary occlusions with angina had, on the average, 2.1 old occlusions per heart, and patients with coronary occlusions without angina also had 2.1 old occlusions per heart. Thus there was no difference in the number of old occlusions per heart in patients with old occlusions with or without angina.

It has often been assumed that patients with angina pectoris have more severe coronary disease than patients with coronary disease without angina pectoris. This thesis finds support in a study by Blumgart, Schlesinger, and Zoll in 1941, in which patients with coronary occlusions with angina had on the average 2.5 occlusions per heart, whereas patients with coronary occlusions without angina had 1.4 occlusions per heart. This difference was not borne out in the present sample.

**Cardiac Hypertrophy**

The heart weight had been recorded in 429 cases. Cardiac hypertrophy was found in 230 or 53.6 per cent of the hearts. Hypertension, valvular disease, or both, furnished a ready explanation for hypertrophy in 140 cases. In the remaining 90 hearts with hypertrophy, coronary occlusions were present in 41, and moderate to severe coronary artery disease was found in 29. Cardiac hypertrophy with little or no coronary artery disease was seen in the remaining 20.

**Congestive Heart Failure**

Severe chronic congestive heart failure had been present in 37 cases, mild to moderate chronic congestive failure in 135. All of these patients were found to have either coronary artery disease of at least moderate severity, or hypertension, valvular disease, severe pulmonary disease, or chronic anemia.

Further analyses of the relationships between cardiac hypertrophy, congestive failure, and coronary artery disease are the subject of a separate communication.
Clinical Diagnosis of Myocardial Infarction

The diagnosis of definite myocardial infarction was confirmed at postmortem examination in 43 of 49 cases (88 per cent) (table 5). In five of the misdiagnosed cases, the false-positive diagnosis was based mainly upon the electrocardiogram. The six cases comprised acute pulmonary embolism, uremia, acute myocarditis, and three patients with acute cerebrovascular lesions, which may have produced the electrocardiographic abnormalities.21

There were 55 patients with a clinical diagnosis of probable myocardial infarction. In 33, postmortem examination confirmed the presence of an infarct. Ten of the 33 also had typical angina pectoris. In nine patients a terminal infarction only was clinically suspected. In only three of these were electrocardiograms taken, which showed in each case nonspecific abnormalities. None of these three had an infarct at postmortem examination. Of the remaining six, two showed healed and one both acute and healed infarcts. Electrocardiograms were taken in 45 of the remaining 46 in this group. These were highly suggestive of myocardial infarctions in 15 with and in one without pathologic evidence of such lesions. Nonspecific electrocardiographic abnormalities were seen in 14 with and in 15 without infarctions. Thus, although the diagnosis of infarction was confirmed in only 60 per cent of the total group classified as probable infarctions, electrocardiographic evidence of infarction was confirmed in 94 per cent.

In 64 of the 140 hearts (46 per cent) with autopsy-proved myocardial infarctions this diagnosis was only questioned or was entirely unsuspected clinically. Forty-eight of 64 (75 per cent) undiagnosed myocardial infarcts were old and healed; 16 (25 per cent) were either acute or healing.

Thus, in the present series, false-positive diagnoses were infrequent, but false-negative diagnoses were common. As one might expect, the fresh or large infarcts were diagnosed with greater accuracy than old or small ones. Myocardial infarcts without occlusions were diagnosed less frequently than myocardial infarcts with occlusions, perhaps, in part, because in general myocardial infarcts without occlusion were small, single, and not accompanied by angina (table 4).

These findings agree with a clinicopathologic study by Johnson and his group22 at the Mayo Clinic, who reported healed myocardial infarcts in 56 of 113 patients (50 per cent) without clinical diagnosis or suspicion of previous myocardial infarction. Furthermore, 25 of 63 patients (40 per cent) who died during acute myocardial infarction were not diagnosed clinically. These authors considered the absence of angina pectoris or of prolonged thoracic pain the most important factor in the failure to recognize healed or acute myocardial infarcts. These conclusions apply well to the present data. Similarly, Paton23 in 1957 reported a diagnostic accuracy of only 44 per cent in a series of 266

Table 5

<table>
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<tr>
<th>Clinical diagnosis</th>
<th>No. cases</th>
<th>Incidence of infarcted hearts at autopsy (%)</th>
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</thead>
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<td>88</td>
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<tr>
<td>Probable MI</td>
<td>35</td>
<td>60</td>
</tr>
<tr>
<td>Questionable MI</td>
<td>112</td>
<td>32</td>
</tr>
<tr>
<td>No MI</td>
<td>214</td>
<td>13</td>
</tr>
</tbody>
</table>
patients thought to have died of myocardial infarction.

A more detailed analysis of this group and of the electrocardiographic data will be the subject of a subsequent communication.

Clinical Diagnosis of Coronary Artery Disease

When a definite diagnosis of coronary artery disease was made (fig. 2), 59 of 69 patients showed occlusive or grade 3 coronary artery disease at autopsy. In four of the remaining 10, the clinical diagnosis was based on a history of angina pectoris only.

A diagnosis of probable coronary artery disease was made in 59, and 35 of these showed occlusive or severe disease at postmortem examination; in two additional patients with lesser grades of coronary disease, myocardial infarctions were present, one recent and one healed. A diagnosis of atypical angina pectoris was the sole criterion for including 14 patients in this category; in 10 of these coronary artery disease was of grade 2 or less.

Of the 302 cases in which clinical coronary disease could at most be questioned, 32 were found to have occlusions and an additional 61 severe obstructive coronary atherosclerosis.

Retrospectively, while a clinical diagnosis of definite or probable coronary artery disease had been made in 94 or half of the 187 patients with occlusions or severe coronary stenosis, in the majority of patients with moderate to severe coronary artery disease, the clinical diagnosis was tentative or not made (188 of 302, or 62.3 per cent).

The clinical assessment of coronary artery disease was based on the clinical presence or absence of myocardial infarction, angina pectoris, or congestive heart failure, according to a set of definitions (v.s.). The most reliable index of the presence of coronary artery disease was typical angina pectoris, followed by myocardial infarction and congestive heart failure in that order. From the point of view of the pathologic findings, occlusive coronary artery disease was the only type diagnosed with reasonable frequency. The clinical evaluation of nonocclusive coronary artery disease was much less accurate.

**Cirrhosis**

Forty-eight patients (11.1 per cent) had cirrhosis of the liver at autopsy (table 6). This group showed a remarkably low incidence of occlusive coronary artery disease and of myocardial infarction. Only one patient had a coronary occlusion, and only two had myocardial infarcts. Furthermore, the degree of coronary artery disease was less in the cirrhotic group than in the noncirrhotic group. The pathologic types of cirrhosis were as follows: nutritional 36, biliary four, unknown or unclassified four, portal two, biliary and nutritional one, and one with question of nutritional or cardiac cirrhosis. The mean age of the cirrhotic group was 62.8 years (range 31 to 85), differing significantly from the mean age of 68.7 years of the noncirrhotic group. Because of this difference, a control group of patients with cancer was matched for age and sex. There was still a significant

---

**Table 6**

<table>
<thead>
<tr>
<th>Pathologic diagnosis</th>
<th>Cirrhotic patients</th>
<th>Noneirrhotic patients</th>
<th>All patients with cancer</th>
<th>Matched patients with cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>48</td>
<td>382</td>
<td>125</td>
<td>48</td>
</tr>
<tr>
<td>Mean age</td>
<td>62.8</td>
<td>68.7</td>
<td>68.6</td>
<td>62.6</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Oclusion</td>
<td>1</td>
<td>102</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>+++</td>
<td>8</td>
<td>76</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>12</td>
<td>100</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>12</td>
<td>43</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>15</td>
<td>61</td>
<td>33</td>
</tr>
</tbody>
</table>

_Circulation, Volume XXVII, February 1963_
difference in the incidence of occlusive coronary artery disease, but there was no difference in lesser degrees of coronary atherosclerosis. Furthermore, individuals with moderate to heavy ingestion of alcohol but without cirrhosis did not differ from the non-drinking individuals in the degree of severity of coronary artery disease.

MacDonald and Mallory in 1958 and Howell and Manion in 1960 reported a low incidence of myocardial infarction in patients with cirrhosis of the liver. These series, however, were not matched for age and sex, and thus the postulate of a specific protective influence of cirrhosis against the development of coronary artery disease deserves re-examination.

**General Discussion**

**Critique of Method**

The method used to evaluate each individual case in this study has advantages as well as disadvantages that must be kept in mind in the evaluation of the results. Some of these have already been discussed. The analysis of clinical data is retrospective and hence potentially incomplete; on the other hand, the data were gathered in a teaching hospital with relatively high uniformity of approach. More sophisticated, specific clinical investigations for the presence of coronary artery disease or myocardial infarcts, such as exercise or anoxia electrocardiograms, in vivo coronary angiography, roentgen-kymography, electrokymography, and serum enzyme studies were not carried out with sufficient frequency to be included in the analysis. The pathologic data have the advantage of having been gathered in a forward-looking manner with techniques that far exceed the extent and accuracy of ordinary pathologic examinations.

The population studied must be recognized as that dying and coming to autopsy in a large municipal general hospital in northeastern United States. The sample analyzed may be considered representative of this population, in which the lower economic strata, the medically indigent, the unemployed, the retired, the unskilled laborers, the chronically ill, and the aged predominate. Again, it must be kept in mind that medicolegal cases, including most sudden deaths on the day of admission to hospital, are not included in this study. Thus, the population studied may not be representative of the population at large, and is probably not representative of deaths at large.

The present study was in part prompted by the recurrent question as to whether the conclusions based upon the only previous studies comparable in method and extent—those of Blumgart, Schlesinger, and co-workers—carried out at the Beth Israel Hospital in Boston—were applicable to the population of Boston at large. The Beth Israel Hospital is a voluntary hospital, with a population biased in favor of members of financially self-supporting families of skilled workers, clerical workers, and businessmen or professionals of the Jewish faith. This then represents a segment of the population to which a preferentially high incidence of coronary atherosclerosis has been attributed. Clearly, the sample from the Boston City Hospital differs in composition from that of the Beth Israel Hospital. Divergencies in the results of studies at these two hospitals may thus reflect differences in the population samples. The fact that the results of these two studies show such substantial agreement, however, may indicate that with respect to coronary artery disease the population of Boston is more homogeneous than had been thought, or else, the true differences, if any, have been reduced in the years intervening between the two studies.

**True Incidence of Coronary Disease**

The high incidence of coronary artery disease in this series, whether manifested by coronary narrowing, occlusion, or myocardial infarction, is striking. Routine autopsy studies underestimate both the incidence and the severity of coronary disease. Our study indicates that clinical evaluation of symptoms and signs and the electrocardiogram significantly underestimate the prevalence and the extent of coronary disease. Thus, clinical, electrocardiographic, or even routine autopsy surveys of population groups cannot be ex-
CORONARY ATHEROSCLEROSIS

expected to yield a true estimate of the prevalence of coronary artery disease.

Compensatory Mechanisms

It has long been controversial whether the human heart is equipped with a collateral circulation, and if so, is innately protected from the effects of arterial obstruction, or whether it can develop such a collateral circulation in adaptive response to disease. The incidence of intercoronary arterial anastomoses in normal hearts, in the absence of known stimuli to their formation, has been a point of much disagreement. The incidence of 10 per cent in the present series is the same as the 9 per cent reported by Zoll, Wessler, and Schlesinger,1 using comparable methods. Other investigations, in particular those by Laurie and Woods,8,9 using different methods, have reported a higher incidence, at least in the Bantu. Similarly, with modified technics, a much higher incidence than those cited above, has been demonstrated in a more recent group of so-called "normal" hearts. There is the strong suggestion that the demonstration of anastomoses, particularly in hearts relatively free from coronary anastomoses, is dependent on the technics used. It should be emphasized however, that postmortem studies cannot evaluate the functional significance of anastomoses only demonstrable by these more specialized technics.

Cardiac hypertrophy may also be considered a compensatory phenomenon, in the case of coronary artery disease compensating for loss of muscle tissue by necrosis and fibrosis. Hypertrophy was frequently associated with severe coronary artery disease, in the absence of hypertension or valvular disease. One wonders to what extent this may be considered an adaptive response and to what extent such hypertrophy causes further stress upon an inadequate coronary circulation, resulting in further damage to the myocardium.

Failure of Compensation

Angina pectoris, the single symptom most diagnostic of coronary artery disease, presumably reflects myocardial anoxia. Again, this study points out that less than one third of patients with coronary occlusions had complained of angina pectoris, but that in the presence of such cardiac pain the likelihood of clinical diagnosis of coronary disease was much greater. Contrary to reports by others, however, our findings suggest that occlusive disease was as severe and widespread in patients without angina as in those who suffered from it.

The high incidence of chronic congestive heart failure in patients with coronary disease—up to 50 per cent for patients with occlusions—that exceeded the incidence of angina pectoris throughout, suggests that congestive heart failure, in the absence of other known cause, should be considered presumptive evidence for obstructive coronary artery disease. Indeed, because of its high incidence, congestive failure may constitute a more important clinical clue to coronary disease than angina pectoris.

Modifying Influences

Youth and the feminine sex, at least up to middle age, appear to afford some protection from coronary disease in this as in other series. Hypertension, at least in women, was associated with more severe coronary disease.

Only 56 patients, or 13 per cent of the series studied, were Negroes. Although this group is small, it did not differ from the group as a whole in incidence of coronary occlusion or myocardial infarction.

The low incidence and mild nature of coronary atherosclerosis in patients with cirrhosis of the liver may reflect mainly the decreased life span of patients so afflicted. In this regard, however, the low incidence of hypertension in cirrhotic patients deserves mention.27

Diagnosis of Coronary Artery Disease

In general, the diagnosis of coronary artery disease is only made in vivo when some breakdown in the coronary circulation has taken place, resulting in angina pectoris, myocardial infarct, heart failure, or marked electrocardiographic changes. In about half the cases of severe obstructive coronary disease, a definite diagnosis could not be made clinically. The diagnosis was made predominantly by
the presence of myocardial infarct or angina pectoris. Furthermore, 46 per cent of the myocardial infarcts could not be diagnosed.

An electrocardiographic diagnosis of definite or probable infarction was proved correct in about 90 per cent. If an infarction was "suggested" by the electrocardiogram, in 82 per cent the diagnosis was confirmed. However, of 44 patients with infarctions clinically only suspected or not diagnosed, whose electrocardiograms were available, 31 showed only nonspecific abnormalities.

Thus, as pointed out above, it becomes necessary to consider congestive heart failure, in the absence of other cause, a presumptive sign of obstructive coronary arteriosclerosis. Even so, 16 per cent of patients with severe obstructive coronary disease would have remained undiagnosed.

Recently developed diagnostic methods may improve the accuracy of diagnoses28-31

Therapeutic Implications

If and when therapeutic measures become available for obstructive coronary arteriosclerosis, whether curative or palliative in the sense of halting the disease process, the correct identification of afflicted individuals will become important clinically. In certain selected populations, military or civilian—e.g., pilots, astronauts—such identification may be important even now.

With respect to direct surgical approaches to coronary occlusions,32 it is pertinent to state that in the present study the findings reported by Blumgart, Zoll, and Kurland32 were borne out: most occlusions were located within 4 cm. of the coronary ostia10 and thus accessible surgically. Occlusions were often multiple, however, and the 103 patients with coronary occlusions had, on the average, 2.1 occlusions. Furthermore, there was a high incidence of myocardial infarct without occlusion. Thus, to find patients with but one occlusion, one may well have to look among the apparently healthy population.

Summary and Conclusions

An unselected series of 430 hearts was studied at the Boston City Hospital by a modified Schlesinger coronary-injection technic combined with meticulous exploration of the myocardium. Independently, the clinical records were reviewed for clinical evidence of coronary artery disease.

The average age was 68 years. There were 238 males and 192 females; 374 whites and 56 Negroes. The over-all incidence of coronary arteriosclerosis was high. Coronary disease was present in 82 per cent of the hearts and was severe in 43 per cent.

The conclusions that can be drawn from this study of 430 hearts are

1. Occlusion of a coronary artery without infarction occurred in 6.4 per cent of the coronary occlusions, but in each case intercoronary anastomoses existed, and these may have been stimulated by pre-existing coronary artery disease.

2. Ninety-nine per cent of hearts with occlusions showed intercoronary anastomoses. The incidence in normal hearts was only 10 per cent.

3. Myocardial infarctions without coronary occlusions occurred in 27 per cent of cases of myocardial infarctions. As a group, they were small and clinically not recognized.

4. The over-all incidence of angina pectoris was 9.5 per cent. Most patients with typical angina pectoris had coronary occlusions or myocardial infarctions. However, the extent of the coronary disease in these patients was no greater than in those with occlusions but without angina.

5. When a definite clinical diagnosis of myocardial infarction was made, the diagnosis was substantiated in over 85 per cent of the cases. Although false-positive diagnoses were rare, false negatives were frequent. Myocardial infarction or severe coronary artery disease was found in 46 per cent and 31 per cent of cases in which the clinical diagnosis was not made or was only questioned. An electrocardiographic diagnosis of definite or probable infarction was proved correct in about 90 per cent. If an infarction was "suggested" by the electrocardiogram, in 82 per cent the diagnosis was confirmed. However, of 44 patients with infarctions clinically only
suspected or not diagnosed, whose electrocardiograms were available, 31 showed only nonspecific abnormalities.

6. When chronic congestive heart failure occurred in a patient without hypertension, valvular disease, severe pulmonary disease, or anemia, the patient was almost always found to be suffering from coronary disease of at least moderate severity.

7. Myocardial infarction and occlusive coronary artery disease were uncommon in 48 patients with cirrhosis of the liver.

Acknowledgment

The authors are indebted to Miss Sandra J. Fish and Mrs. Olga F. Connolly, who prepared the injected specimens, and to Miss Rita M. Lavin, who reviewed the electrocardiograms.

References


René Théophile Hyacinthe Laènnec was born on the 17th February 1781, the year which saw Johnson's Lives of the Poets, and the second and third volumes of Gibbon's Decline and Fall. Wordsworth was a lad of eleven. Napoleon, a little older, was already two years on with his military education at Breinée. John Hunter was in his prime at fifty-three. Seven years before, Priestley announced the discovery of oxygen. Albrecht von Haller, the "prince of physiologists," died four years ago. Morgagni had already been dead ten years. But the most important date near by was that, nineteen years earlier, on which Rousseau's Contrat Social appeared; and his opening words, "Man is born free and is everywhere in chains" had not been lost upon his generation. Adam Smith had taught something of the wealth of nations; Voltaire had outraged established orders and amused the others; and Burke was still in his grandest vein. No one had any reason to suppose that the infant son of a Breton country lawyer was destined to reach an equally enduring fame. Certainly the good people of Quimper, the little port about thirty miles from Brest, could not have guessed. For the Llaènnecs, though respectable Celts and reputable lawyers, had never achieved anything but a local name; and in point of fact, René's father was a rather shiftless improvident character who neglected his family and lived on his sons later in life.—Dr. Clifford Hoyle (Brit. J. Tuberc., 1944). The Quiet Art: A Doctor's Anthology. Compiled by Dr. Robert Coote. Edinburgh & London, E. & S. Livingstone Ltd., 1952, p. 82.
Clinicopathologic Correlations in Coronary Atherosclerosis: Four Hundred Thirty Patients Studied with Postmortem Coronary Angiography
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