# CORONARY EMBOLISM IN BACTERIAL ENDOCARDITIS *

JOEL G. BRUNSON, M.D.
*(From the Department of Pathology, University of Minnesota Medical School, Minneapolis 14, Minn.)*

Certain diseases of the coronary arteries, such as thrombosis, are well established clinical and pathologic entities, but coronary embolism has received comparatively little attention and, indeed, even its occurrence has been doubted by certain writers.

Gallavardin and Dufourt,[1] in reporting a case in 1913, stated that embolism of the coronary arteries was one of the most exceptional of events. They attributed this to the angle at which the vessels left the aorta, their dimensions, and the speed and force of blood flow past the vessels. Coombs,[2] however, in 1922, reported that the myocardial lesions in bacterial endocarditis are almost always due to emboli. In 1935 Hoseason[3] wrote, "Coronary embolism is extremely uncommon; the probabilities are so strongly against an embolus of suitable size being swept by the violent aortic stream into a coronary artery that it is remarkable that it should occur at all." He believed that the ostia of the coronary arteries would be more or less covered during systole by the aortic valve cusps and that the rush of the aortic blood would sweep any loose fragments well past the coronary openings before their diastolic filling began.

The purpose of this paper is to review the literature concerning the frequency of coronary embolism in bacterial endocarditis and to report the study of 9 successive cases of bacterial endocarditis seen in the Department of Pathology of the University of Minnesota between October, 1951, and July, 1952.

## LITERATURE

In 1933 Saphir[4] published an extensive historical review of the subject of coronary embolism in which he collected all of the reported cases beginning with one described by Virchow in 1856. He found a total of 11 acceptable cases and added 3 of his own. Certain obvious criteria, specifically the absence of intrinsic coronary disease and the presence of a source from which an embolus might arise, were emphasized as being of value in separating thrombosis from embolism. Since then there have been scattered reports of coronary embolism appearing in the literature. Most of these (Garvin and Work,[5] Hamman and Rich,[6] Latscha *et al.*,[7] Moragues *et al.*,[8] and Parks[9]) have dealt with

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one or two cases and all but one (Moragues *et al.*) have been associated with bacterial endocarditis. Hamman, in 1941,[10] referred to 40 cases of coronary embolism of which 19 had been reported as occurring in bacterial endocarditis.

Certain other papers have dealt with larger numbers of cases. Saphir,[11] in 1935, reported that he had found coronary emboli microscopically in 18 of 35 cases of bacterial endocarditis, with small infarcts in 28 of these cases. De Navasquez,[12] in 1939, reported finding emboli microscopically in the small branches of the coronary arteries in 16 of 20 cases of bacterial endocarditis. Saphir, Katz, and Gore,[13] in 1950, reviewed 76 cases of subacute bacterial endocarditis and reported that the microscopic sections in 36 of these showed small areas of ischemic necrosis in the myocardium. Of these, 17 also showed embolic material in the small coronary divisions.

Saphir,[14] in 1946, reported a "granulomatous" lesion in the myocardium of 4 patients previously treated for bacterial endocarditis. This was described as having a calcific center with a surrounding cellular reaction of lymphocytes and giant cells of foreign body type. Perry, Fleming, and Edwards,[15] in 1952, reported a similar lesion in one treated case of bacterial endocarditis. In their series of 52 cases, microscopic sections revealed emboli in the small branches of the coronary arteries in 20 cases.

Cates and Christie[16] (1951), in reporting the results of penicillin therapy in bacterial endocarditis, discussed 442 cases. Of these, 164 were diagnosed during life as having major arterial embolism, of which 8 were believed to have coronary emboli. Of the total number of patients, 195 died as a result of the disease, and 89 were necropsied. Of these, 12 (13 per cent) had macroscopic evidence of coronary embolism.

The pertinent findings concerning these reports are summarized in Table I. Certain overlapping of figures is almost inevitable because of sparcity of details in some reports, but it may be seen from Table I that of all cases of coronary embolism reviewed, including both large and small branches of the coronary arteries, 155 cases (80 per cent) have been associated with bacterial endocarditis. It may also be noted that, in relation to the total cases of bacterial endocarditis studied with respect to the occurrence of coronary emboli, these have been detected in slightly less than 40 per cent of the cases.

If one limits the reported cases to those of bacterial endocarditis in which detailed studies of the myocardium were carried out (Saphir,[4,11,13,14] de Navasquez,[12] and Perry[15]) 183 cases fall into this

category. Of these, the most frequently reported lesion has been that described as the miliary infarct. It occurred in 111 cases (60 per cent), while small emboli were detected in 72 cases (slightly less than 40 per cent).

## MATERIALS

The materials used in this study consisted of the hearts from 9 successive cases of bacterial endocarditis which were seen in the University of Minnesota Department of Pathology between October, 1951, and July, 1952. The study was directed toward the gross and microscopic demonstration of emboli within the large and small branches of the coronary arteries. In this paper small refers to the direct epicardial branches of the coronary arteries and not to the very small intramural branches. No particular effort was made to demonstrate emboli within the latter.

TABLE I
*Summary of Reviewed Cases*

| Author | Year | Cases | Infarcts | | Emboli | | Arteritis |
|---|---|---|---|---|---|---|---|
| | | | Large | Small | Large | Small | |
| Gallavardin and Dufourt[1] | 1913 | 1 | 1 | | 1 | | |
| Coombs[2] | 1922 | 20 | | 1 | | 3 | 3 |
| Saphir*[4] | 1933 | 14 | 3 | | 14 | | |
| Hamman and Rich[6] | 1933 | 2 | | 1 | | 1 | |
| Hoseason[3] | 1935 | 1 | | | 1 | | |
| Saphir[11] | 1935 | 35 | | 28 | 1 | 18 | 11 |
| de Navasquez[12] | 1939 | 20 | 1 | | 1 | 16 | 9 |
| Garvin and Work[5] | 1939 | 3 | | | 3 | | |
| Hamman†[10] | 1941 | 40 | 6 | 1 | 18 | 20 | |
| Parks[9] | 1942 | 1 | 1 | | 1 | | |
| Saphir[14] | 1946 | 4 | | | | 4 | |
| Latscha *et al.*[7] | 1949 | 2 | 1 | | 2 | | |
| Moragues *et al.*[8] | 1950 | 1 | 1 | | 1 | | |
| Saphir *et al.*[13] | 1950 | 76 | | 36 | | 17 | |
| Cates and Christie[16] | 1951 | 89 | 10 | | 12 | | 2 |
| Perry *et al.*[15] | 1952 | 52 | | 47 | | 21 | 4 |
| Totals | | | | | | | |
| A. All above | | 361 | 24 | 114 | 55 | 100 | 29 |
| B. Endocarditis, omitting repetitions and statistic analyses | | 316 | 13 | 113 | 45 | 80 | 29 |

* Historical review of incidence of coronary embolism without specific references to gross or microscopic changes in myocardium except in Saphir's own cases.

† General review of causes of coronary embolism without reference to myocardial changes. Source of two emboli not mentioned.

## Methods of Study

Following the removal and opening of the heart at necropsy, the entire specimen was fixed in 10 per cent formalin. The coronary arteries were then cut transversely at a distance of not more than 3 mm. between sections with a sharp knife. This procedure frequently required from 1½ to 2 hours for a single specimen. After gross sectioning and selection of those vessels which appeared to be occluded, the resulting blocks were embedded in paraffin, sectioned serially at 7 $\mu$, and every fifth section mounted. At the same time, routine blocks were cut from the myocardium and the involved valves, the former consisting of from three to five blocks from different areas depending on the gross appearance. All sections were stained with hematoxylin and eosin and, in addition, certain sections of the valves and vessels were stained by the Gram-Weigert method.

## Observations

The pertinent gross findings in my cases are summarized in Table II. Of particular interest are the facts that in all but one case (no. 4) there were multiple areas of scarring in the myocardium and, in one case (no. 8) there were multiple areas of recent infarctions 3 to 4 cm. in diameter. Two (cases 1 and 2) showed also hard, calcific masses in the myocardium; these will be discussed with the histologic findings. As may be noted in Table II, emboli were detected in 7 cases, and in 4 (cases 1, 4, 6, and 8) multiple occlusions were noted.

Microscopically, the sections of myocardium showed definite alterations in every case. Areas of ischemic necrosis were noted in all but one (no. 4) and these showed varying degrees of resolution and replacement fibrosis (Fig. 1). These changes were particularly prominent and variable in those cases in which multiple emboli were detected grossly and in one additional case (no. 5) in which multiple emboli were noted within the intramural branches of the coronary arteries (Fig. 2). In 3 cases multiple abscesses were noted in the myocardium (nos. 4, 8, and 9). Areas of recent necrosis of muscle fibers, associated with granulocytic and mononuclear cellular infiltration, were noted in 4 cases. No particular attempt was made to determine the presence of Aschoff bodies in the myocardium and consequently small perivascular areas of scarring were not given special emphasis.

In 2 cases, as noted previously (nos. 1 and 2), calcific densities, or granulomas as they have been called by other writers, were noted within the myocardium. In one (case 2) this lesion was rather large and was located near the endocardial surface. Its exact relationship

to a vessel could not be determined and there was little cellular reaction about the calcium (Fig. 3). By the Gram-Weigert method of staining, bacteria were noted in clumps about the periphery of this lesion. In the other case, however, it was possible to demonstrate the relationship of the calcium to a vessel by serial sections, and particles of this material were found in the lumen of the vessel as well as in an extravascular location within the myocardium. In this lesion bacteria were present in large numbers and there was a marked cellular reaction which consisted of neutrophils, lymphocytes, plasma cells, and a few multinucleated giant cells (Figs. 4 and 5).

In another case (no. 9) a large subendocardial lesion was noted which bore no demonstrable direct relationship to a vessel. This lesion consisted of an area of muscle destruction associated with a marked

TABLE II
*Gross Pathologic Findings*

| Case | Age | Sex | Weight of heart | Valvular involvement | Myocardium | Emboli | Other |
|---|---|---|---|---|---|---|---|
| | *yrs.* | | *gm.* | | | | |
| 1 | 16 | M | 900 | Mitral, aortic | Large areas of scarring | + | Rheumatic mitral and aortic valves |
| 2 | 37 | M | 700 | Pulmonary, aortic, mitral | Small scars | + | Rheumatic pulmonary, mitral, aortic valves; interventricular septal defect |
| 3 | 26 | F | 350 | Mitral, aortic | Petechiae, large areas of scarring | − | Mild rheumatic mitral and aortic valves |
| 4 | 56 | M | 460 | Mitral | Perforated, no gross areas of fibrosis | + | Valves not grossly rheumatic |
| 5 | 32 | F | 275 | Aortic | Large scars | + | Mild rheumatic mitral and aortic valves, gastric carcinoma |
| 6 | 54 | F | 420 | Aortic | Small scars | + | Valves not grossly rheumatic, pancreatic carcinoma |
| 7 | 25 | F | 440 | Mitral, perforated leaflet | Petechiae, large scars | − | Mild rheumatic mitral valve |
| 8 | 50 | M | 740 | Aortic | Petechiae, fresh areas of infarction | + | Valves not grossly rheumatic, portal cirrhosis |
| 9 | 60 | F | 354 | Mitral | Multiple small, fresh infarcts | + | Valves not grossly rheumatic |

cellular reaction of neutrophils and lymphocytes. There also appeared to be early calcium deposition in the lesion, although specific stains were not carried out. It would seem, from the appearance of this lesion and that first described, that both were the result of healing of large abscesses within the myocardium, although the smaller lesion observed in case 1 appeared to be directly related to previous closure of a vessel with a calcific embolus. In each of these 3 cases penicillin had been employed in treatment of the disease.

TABLE III
*Microscopic Findings*

| Case | Granulomas | Infarcts | | | | Emboli | | | | Arteritis |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Recent | Old | Large | Small | Calcific | Bland | Septic | Bacteria | |
| 1 | + | + | + | + | + | + | + | − | + | + |
| 2 | + | − | + | − | + | − | − | + | − | − |
| 3 | − | + | + | + | + | − | − | − | − | − |
| 4 | − | − | − | − | − | − | − | + | + | + |
| 5 | − | − | + | + | + | − | + | − | − | − |
| 6 | − | + | + | + | + | − | + | − | − | − |
| 7 | − | + | + | + | + | − | − | − | − | − |
| 8 | − | + | + | + | + | + | − | + | + | + |
| 9 | − | + | + | − | + | + | + | − | − | − |
| Totals | 2+, 7− | 6+, 3− | 8+, 1− | 6+, 3− | 8+, 1− | 3+, 6− | 4+, 5− | 3+, 6− | 3+, 6− | 3+, 6− |

Microscopically, none of the vessels showed any significant degree of atherosclerosis, and a study of serial sections of the vessels showed them to contain material which was similar to that on the valve. These emboli were designated as being bland or septic, although it must be admitted that the distinction in some cases was more or less arbitrary and was dependent on which particular section one chose and the manner in which the vessel was sectioned. In 3 of the cases bacteria were noted within the emboli. These were in large clumps in 2 instances (Figs. 6 and 7).

In one case (no. 4), in which ACTH and cortisone were given during the course of the disease, the emboli were septic and there was a pronounced arteritis with partial necrosis of the vessel wall. In 2 other cases varying degrees of arteritis were noted and in case 8 it was particularly striking, with almost complete necrosis of a portion of the media (Fig. 7). In case 9, in which a single injection of ACTH was given, the emboli were bland and there was no evidence of arteritis. In this particular case the emboli were noted to contain rather large masses of calcium surrounded by thrombotic material (Fig. 8).

In many instances sections revealed what appeared to be a sudden distention of the lumen of the vessel when the largest diameter of the embolus was reached, and this was particularly noticeable when the embolus lodged near a bifurcation of the vessel. It was noted that embolic material stopped rather sharply at the point of division, not extending down into the junctional vessel for any appreciable distance.

In 3 cases (nos. 1, 5, and 6) there was evidence of organization of the emboli and in case 1, in particular, there was a marked degree of

TABLE IV
*Clinical Summary*

| Case | Diagnosis | History | Electrocardiograms | Blood culture | Drugs received | Death |
|---|---|---|---|---|---|---|
| 1 | Rheumatic heart disease, bacterial endocarditis | Rheumatic fever | Tachycardia, auricular fibrillation, right and left ventricular strain | Sterile | Penicillin Digitoxin | Sudden |
| 2 | Congenital heart disease, mitral stenosis | Rheumatic fever | None | None | Penicillin Digitoxin | Sudden |
| 3* | Rheumatic heart disease, bacterial endocarditis | Rheumatic fever | Prolonged P-R depression ST, 1 & 2; V, 4 & 6 | *Streptococcus fecalis* $X_2$ | Penicillin Aureomycin Terramycin | Progressive |
| 4 | Pemphigus, bacterial endocarditis | | None | Coagulase-positive staphylococcus | (ACTH) Penicillin Streptomycin Dicumerol | Sudden |
| 5 | Undetermined | 13 mos. post-partum | None | None | No specific therapy | Sudden |
| 6 | Diabetes, portal cirrhosis | Diabetes and hypertension for 2 yrs. | Abnormal, no specific T wave changes | None | No specific therapy | Progressive |
| 7* | Rheumatic heart disease, bacterial endocarditis | Rheumatic fever | Left ventricular strain | *Staph. aureus* | Penicillin Streptomycin Aureomycin Bacitracin Digitoxin | Sudden |
| 8 | Portal cirrhosis, bacterial endocarditis | | A-V dissoc., premature ventricular contraction | Species of staphylococci | Penicillin Streptomycin Aureomycin Digitalis | Progressive |
| 9 | Bacterial endocarditis | | Posterior infarction | Hemolytic staph., coagulase-positive | Penicillin Aureomycin Streptomycin Terramycin (ACTH, 25 mg.) | Progressive |

* Emboli not detected.

organization with no evidence of intimal atherosclerosis; and with a normal appearing media beyond the limits of the embolus. Cross sections of a similar vessel showed that organization was progressing from all portions of the intima in contrast to the manner of organization of a thrombus associated with atherosclerosis.

Table III summarizes the salient histologic findings in these cases.

The clinical histories and diagnoses are summarized in Table IV. It is of interest that in almost 50 per cent of the cases there was historical evidence of previous rheumatic heart disease. As may be noted, 7 of the patients received penicillin and 5 of these received one or more other antibiotic drugs. Also, 4 patients showed clinical evidence of cardiac decompensation and were digitalized.

No correlation could be noted between the occurrence of bland or septic emboli in regard to treatment, although in one case (no. 4) which has been referred to previously, in which ACTH and cortisone were given, the emboli were septic and were associated with pronounced arteritis. In this particular case the inflammatory reaction apparently progressed rapidly, with myocardial perforation and cardiac tamponade.

There were no constant changes in the electrocardiograms which would lead one to suspect that occlusion of a branch of a coronary artery had occurred, only one case (no. 9) demonstrating changes suggestive of infarction.

In 5 cases death appeared to be of a sudden nature, and in one (case 5) in particular, sudden death was the basis for a post-mortem examination.

## Summary and Conclusions

Nine cases of bacterial endocarditis which have been studied from the standpoint of coronary embolism are reported. In 7, emboli were demonstrated grossly in the epicardial branches of the coronary arteries, and in 4 of these multiple occlusions were noted. Gross changes were noted in the myocardium in all cases. These consisted of petechial hemorrhages, scarring, areas of recent infarction, and perforation of the myocardium. The finding of scars and recent infarcts stands in direct contrast to most reported observations. Two cases had the calcific masses in the myocardium which have been called granulomas by other writers.

Microscopically, in 5 cases emboli were noted in the intramural branches of the coronary arteries in addition to those described grossly, and small and large areas of ischemic necrosis were noted in all but one case. The latter finding is in accord with most reported cases, but

contrasts sharply with the report of Coombs[2] who stated that he examined 274 sections from the left ventricle in a single case of bacterial endocarditis and found only 20 small areas of fibrosis; and with de Navasquez,[12] who found only one infarct in a series of 20 cases in which he reported detailed histologic alterations in the myocardium.

It is believed that coronary embolization in bacterial endocarditis is a common occurrence, and indeed, probably one of the more common complications of the disease. As to the various theories concerning the improbability of embolism in these vessels, it seems more reasonable to conclude that the location of the arteries, the mechanics of blood flow past them, and the manner of opening of the aortic valve cusps aptly predispose them to embolization in this condition or in any other in which small particles are free in the blood stream emitted from the left ventricle.

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[ *Illustrations follow* ]

## LEGENDS FOR FIGURES

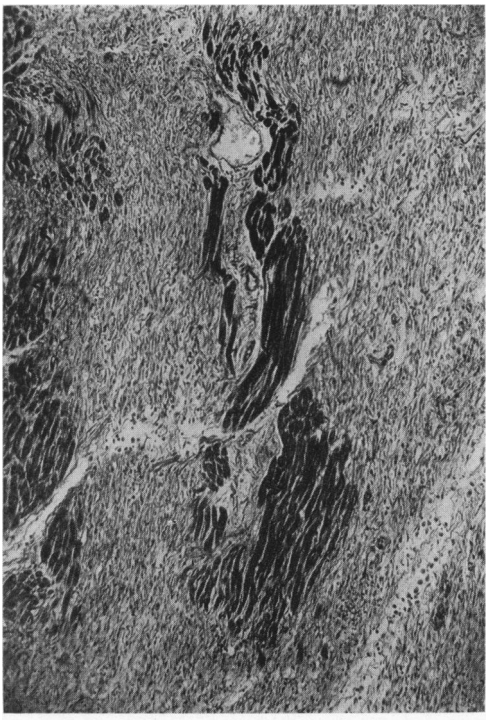
All sections were stained with hematoxylin and eosin, unless otherwise specified.

FIG. 1. Case 5. Large area of ischemic necrosis of the myocardium subsequent to occlusion of a branch of the coronary arteries by an embolus. Small islands of muscle tissue in immediate relationship to intramural branches have survived. × 65.

FIG. 2. Case 5. An embolus within an intramural branch of the coronary arteries. This case demonstrated multiple gross occlusions of the epicardial branches as well as showing intramural emboli microscopically. × 150.

FIG. 3. Case 2. "Granulomatous" lesion located near the endocardial surface and consisting of a calcific center with little surrounding cellular reaction. Bacteria were demonstrated at the periphery of this lesion by the Gram-Weigert stain. × 33.

FIG. 4. Case 1. Similar, smaller type of "granuloma" in direct relationship to a vessel and showing pronounced cellular reaction with multinucleate giant cells. × 33.



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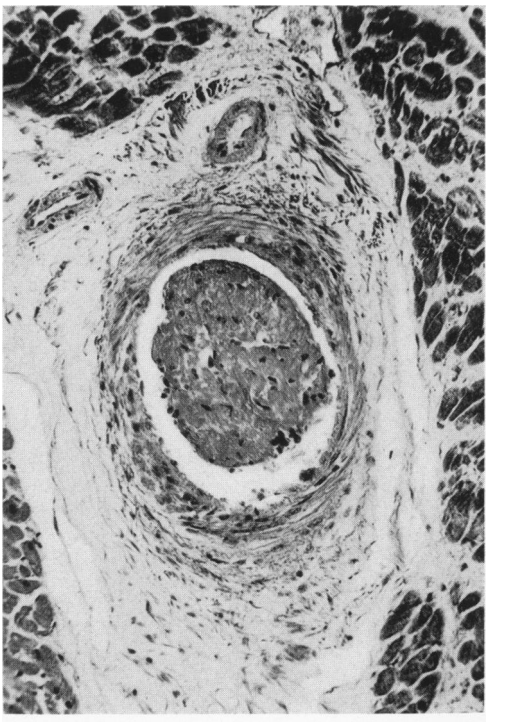

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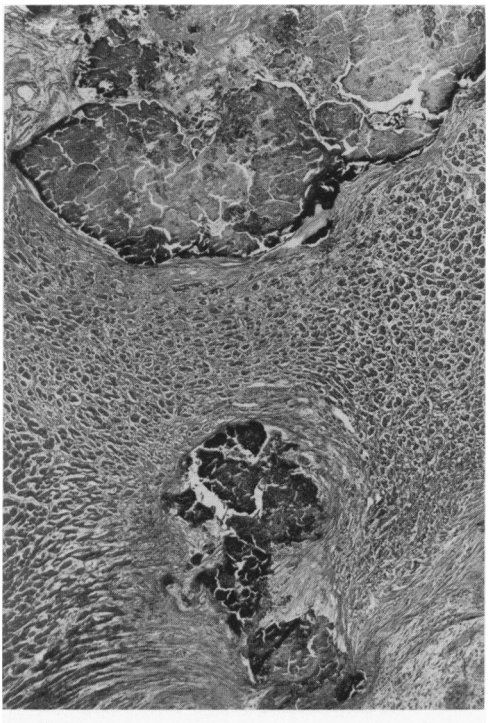

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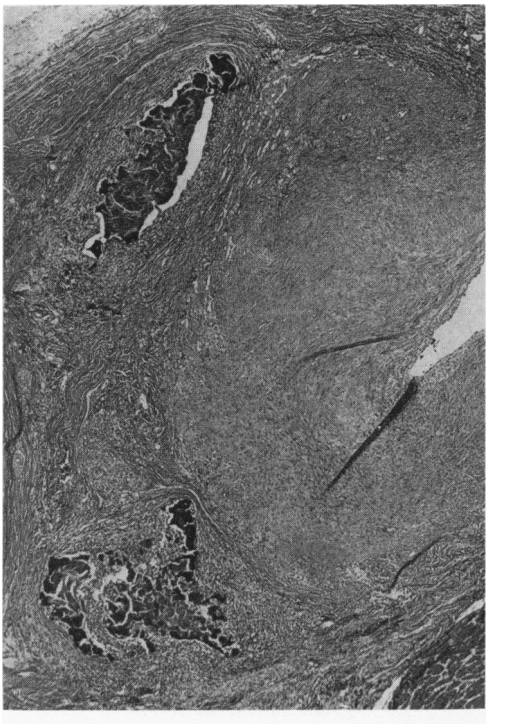

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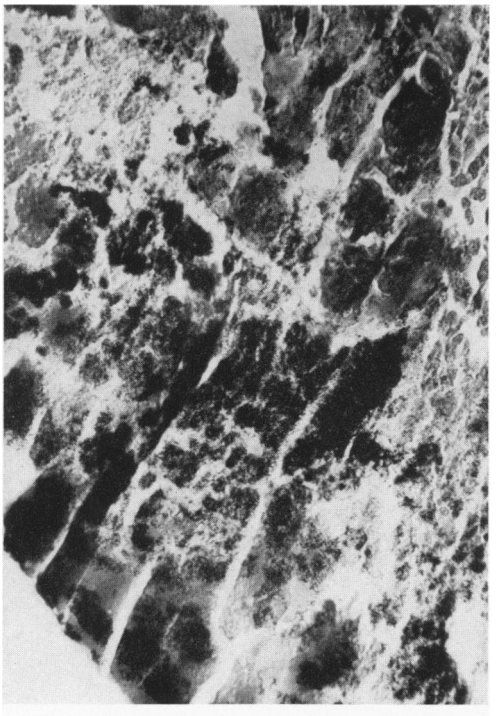
FIG. 5. Case 1. Higher magnification of an area from the previous lesion stained by the Gram-Weigert method, and showing large clumps of bacteria. × 250.

FIG. 6. Case 5. Bland embolus within an epicardial branch of the coronary arteries. The vessel shows no microscopic evidence of intimal thickening. × 33.

FIG. 7. Case 8. Septic embolus within the lumen of an epicardial coronary artery. There are large clumps of bacteria within the embolus, and there is pronounced arteritis with partial necrosis of the media. × 33.

FIG. 8. Case 9. Embolus containing particles of calcium within an epicardial coronary artery. × 33.



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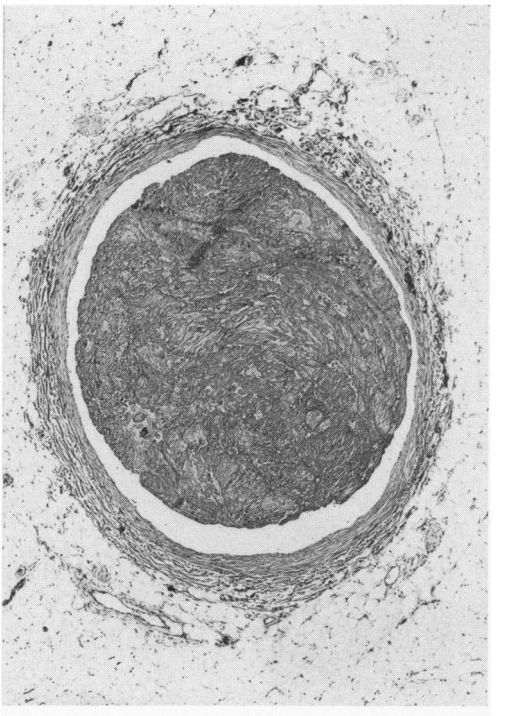

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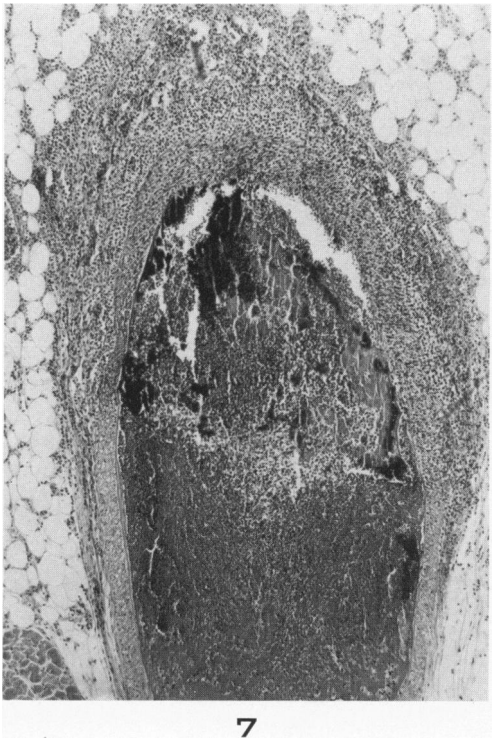

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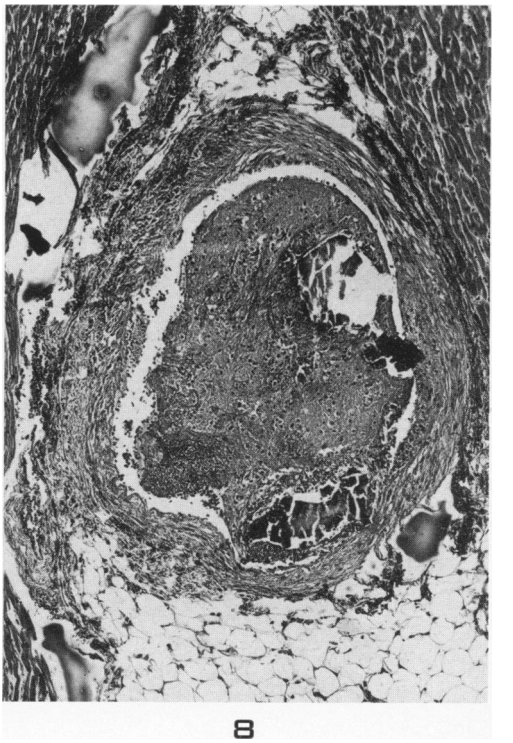

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