THE PATHOGENESIS OF A CORONARY THROMBUS

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Considerable argument still flourishes concerning the exact relationships which exist between coronary artery thrombosis and atherosclerosis and, more recently, even between thrombosis and infarction. Nevertheless, almost every investigator, whatever his views about the preceding relationships may be, would agree that if thrombosis in coronary vasculature could be prevented, the mortality rate of ischemic heart disease would dwindle promptly. Despite the almost universal acceptance of this last assumption, few investigators and even fewer clinicians today are confident about the accuracy of their conception of the factors responsible for or involved in this justly dreaded accompaniment or complication of coronary atherosclerosis. Crawford[1] recently implied the existence of this defect in our knowledge when he wrote that almost nothing new has been learned about coronary thrombosis since 1888. The failure to determine fully the pathogenesis of coronary thrombosis, however, has not been due to a dearth of studies designed to obtain additional data. Thus a number of investigations[2–6] have concerned themselves with the various circulating blood elements possibly involved in thrombosis and others[7–13] with the rheologic qualities of blood perfusing the coronary vasculature.

However important these studies may prove to be, the precise local anatomic and biochemical factors immediately preceding, accompanying and possibly responsible for thrombosis in a given coronary artery remain unrecognized by investigators and clinicians. Certainly it is not enough to know that coronary thrombosis almost invariably occurs in an atherosclerotic artery. What must be learned is what new changes evolve to induce a thrombotic accident in an artery diseased for many years. Until such precise knowledge is gained, any concept dealing with coronary thrombosis cannot possess the anatomic and biochemical solidity it requires for its essential accuracy and general acceptance.

Only a small number of investigators, however, have studied the thrombosed coronary artery in its entirety by serial section technique, although various pathologists[14–16] have insisted that any method less

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inclusive would lead to insufficient and even erroneous conclusions. Moreover, the few who have attempted studies in this manner are far from agreement in respect to their interpretations of the phenomena observed. Several investigators who have employed serial section techniques[14,17,18] have concluded that erosions or fissures on the intimal surface of the artery initiate the thrombotic process. Others,[15,19–22] however, have concluded that an intramural hemorrhage usually initiates the process leading to thrombosis. Finally, although Leary[23,24] apparently did not study serial sections, he, nevertheless, felt that rupture of an intramural atheromatous 'abscess' was the chief cause of coronary thrombosis.

Several years ago, we realized that because of the divergence of opinions, we were unable to obtain any clear conception of the actual mechanisms leading to and locally involved in the formation of a coronary thrombus. We decided, therefore, to submit a number of intact thrombosed coronary artery segments to serial section and various histochemical procedures. The results of the first phase of this study are reported below.

Methods

Forty thrombosed coronary artery segments were obtained from 40 patients who ostensibly died because of the occurrence of this lesion. The average age of the patients (37 of whom were male) was 58 years (range, 27 to 86 years). Eighteen were 55 years of age or younger. Two of the 40 subjects were known to have had diabetes.

This study was accomplished with the cooperation and assistance of 4 pathologists in several general hospitals. They, pursuant to our wishes, carefully examined the coronary vasculature of all patients suspected of dying as a result of acute or subacute coronary artery thrombosis. When a thrombus was observed, they carefully removed not only the occluded segment of the affected artery but also portions of the same artery 2 to 4 mm proximally and distally to the occluded area. The segment then was placed in formalin and dispatched to us for further study. The same pathologists also made available to us their observations concerning the state of the remaining coronary arteries and of the myocardium in each of the patients. Finally, we perused the records describing the terminal illness in each of the patients. One of us (M.F.) attended the necropsy in 10 of the 40 cases and removed the thrombosed segment of the affected artery.

Each arterial segment (10 to 30 mm) after its receipt by us was inspected with a dissecting microscope. Its transversely sectioned proximal and distal ends first were viewed to determine the amount of luminal closure caused by the atherosclerotic plaque which was present in all. These plaques were scrutinized in turn for the presence of calcification, foci of necrotic debris or extravasated blood. Then the lodgement of the thrombus was viewed by gently lifting the segment first at its proximal and then its distal end, toward the vertical and focusing the lens further down along the lumen. In most cases, diagrams were made of the lumen, the encroachment by the plaque and the site of the thrombus within the undisturbed portion of the segment.

After these initial studies, the segments were decalcified by immersion for 48 hours in formic acid solution (5 per cent) and, except when sections were to be stained with Sudan IV, embedded in paraffin and sectioned in step-wise manner.

Initially, sections (cut transversely in 37 of the 40 samples) were obtained at intervals of 50 μ. It soon became obvious, however, that all relevant data could be obtained if sections obtained at intervals of 100 μ were examined. Accordingly in the last 35 cases only two contiguous serial sections at intervals of 100 μ were saved. One of these was stained immediately and the other was saved for later special staining.

Most sections were stained with Mallory's phosphotungstic acid, hematoxylin (PTAH) stain except for several sections at approximately the beginning, middle and end of each sample which were stained with hematoxylin and eosin. Seven of the segments were stained with Sudan IV, despite the fact that freezing and sectioning of them frequently fragmented or otherwise destroyed the thrombus. Approximately 150 serial sections were studied in each artery.

The sections were examined first by one of the authors who, besides taking notes, also drew rather detailed sketches of any important changes observed in either the vessel itself or the thrombus as the successive sections were viewed. Then employing these notes and sketches, the findings were summarized in a final composite drawing. The same sections were then again examined independently in similar fashion by the second author. Disagreements in interpretation were rare, but when they did arise, the sections were presented to one of several independent pathologists for resolution.

Results

Although the prime purpose of this study was to determine only one fact about coronary thrombosis, namely the process responsible for the formation of the thrombus, certain other clinical and pathologic data were obtained and will be briefly described.

The time elapsed between onset of symptoms and death was ascertained accurately in 32 of the 40 cases. Eleven patients died instantly or in a few minutes, without prior related illness or symptoms. Four died 1 to 3 days; six, 4 to 7 days; eight, 8 to 14 days; and three, 15 to 28 days after the onset of chest pain, dyspnea or collapse.

In 28 cases (70 per cent) an acute myocardial infarction was identified. An old infarction was found in addition in 8 of these. Eight of the 12 hearts not containing an acute infarct (in 7 of these 8 the patients had died seconds or minutes after the onset of symptoms) nevertheless did have one or more well healed, old infarcts.

The left coronary artery and its main branches was the site of acute thrombosis in 22, and the right coronary artery and its branches in the remaining 18 cases. Regardless of which artery was found to be the seat of acute thrombosis, the site of thrombosis was rarely more than 1 to 3 cm distal to the coronary ostium. It is of interest that intramural hemorrhage in addition to coronary thrombosis was recognized grossly in 11 of the 40 cases.

In 19 of the hearts complete or almost complete atherosclerotic occlusion was observed in one or more main coronary branches besides the one with thrombosis.

Dissecting Microscopic Examination

The most common finding prior to fixation was the presence of calcification. Regardless of the age of the patient, some degree of calcification (usually severe) was found in the wall encompassing the thrombus within the lumen. These areas or strata of calcification, while usually situated deeply, frequently lay in close proximity to the lumen.

Because great care was taken during this phase of the examination not to disturb the total structural integrity of either the artery or the thrombus, the latter was studied only by viewing it from either the proximal or the distal end of the segment. This made exact analysis of even its gross characteristics difficult. But in over half of the specimens, the thrombus was observed to be composed of not just blood elements but also of greyish-yellow pultaceous material whose direct contact with necrotic areas in the arterial wall could occasionally be discerned. Thrombosed arterial segments containing these 'grossly' recognized heterogeneous thrombi had on occasion been considered at necropsy to represent 'coronary thrombosis with intramural hemorrhage.'

In all 40 specimens the proximal and distal ends (which were not involved in the thrombosis) were markedly narrowed (50 per cent or more). Moreover, when it was possible to peer further into the artery from either of its ends, the lumen was invariably further encroached upon either concentrically or eccentrically by a plaque.

Microscopic Study of the Thrombus-Free Portion of the Arterial Segments

The gross evidence of long-standing arterial disease was confirmed in every case on microscopic scrutiny. Invariably the original lumen was narrowed severely (Fig. 1) by the luminal extension of degenerating arterial tissue. The more peripheral portions of this tissue (i.e., the area immediately adjacent to and frequently merging with the tunica media) were composed of a mixture of connective tissue and spindle cells. The medial and adventitial origin of these cells together with their accompanying blood vessels was usually readily apparent (Fig. 2) in serial sections. The inner area (i.e. the portion encircling or abutting upon the lumen) was, however, usually composed of dense, usually hyalinized or even necrotic, fibers (Figs. 1 and 3).

Areas of calcification varying greatly in size were observed in each of the 40 arterial segments. Sometimes the calcific deposits were embedded and relatively isolated within the thickened fibrous tissue of plaques (Fig. 1). Usually, however, the mineralization appeared in close proximity to foci of necrosis.

Degenerative or necrotic areas consisting of a pultaceous mixture of cholesterol crystals, lipid, cellular debris and macrophages were observed in the atherosclerotic plaques in all 40 arterial segments. These "atheromatous abscesses" varied markedly in number, size, position and contour. Many were relatively small (Figs. 1 and 2); others were so large that they occupied 30 per cent or more of the entire plaque (Figs. 3 and 4). Some were situated relatively deeply within the thickened wall (Figs. 1 and 2), whereas others extended to the endothelium (Figs. 3 and 4). Frequently one "abscess" was observed to have connections with others situated either further along the length of the segment or in the more peripheral portions of the plaque (Figs. 3 and 4).

The debris on the atheromatous abscesses was probably derived from necrotic macrophages and fibrous tissue and stained irregularly with Sudan IV. A considerable amount of the sudanophilic material was extracellular but many macrophages contained lipid as well. These cells, while distributed throughout the interior of the abscess, could nevertheless be most clearly discerned lining its inner surface.

The derivation of these macrophages from adventitial sources was easily perceived on study of the serial sections. The lipophages appeared to surround and also to penetrate the hyaline portions of the plaque itself. Seemingly intact hyaline tissue adjacent to or even at a considerable distance from necrotic areas was invaded by foam cells. The probable importance of this infiltration will be elaborated upon below when the thrombosed portions of the arteries are described. The vascular supply of the abscesses was usually confined to their lateral boundaries (Figs. 2 and 22). Blood vessels of significant size, however, were rarely observed within the abscess or in the hyalinized lumen wall separating it from the lumen.

It is important to point out that none of the abscesses in portions of the artery unrelated to thrombosis ever exhibited hemorrhage or a positive iron stain.

In 13 of the 40 specimens one or more circumscribed areas of canalization appeared in the atherosclerotic tissue impinging upon the lumen. It is of interest that each of the hearts from which these specimens were obtained contained an old infarct.

Microscopic Examination of the Thrombus-Bearing Portions of the Thrombosed Arterial Segments

The most striking characteristic in the thrombus-bearing portions of the vessels was the direct communication (Figs. 3 to 10 and Figs. 23 to 33 incl.) between the occluding thrombus and the atheromatous abscess in the plaque. A communication of this nature was observed in 39 of the

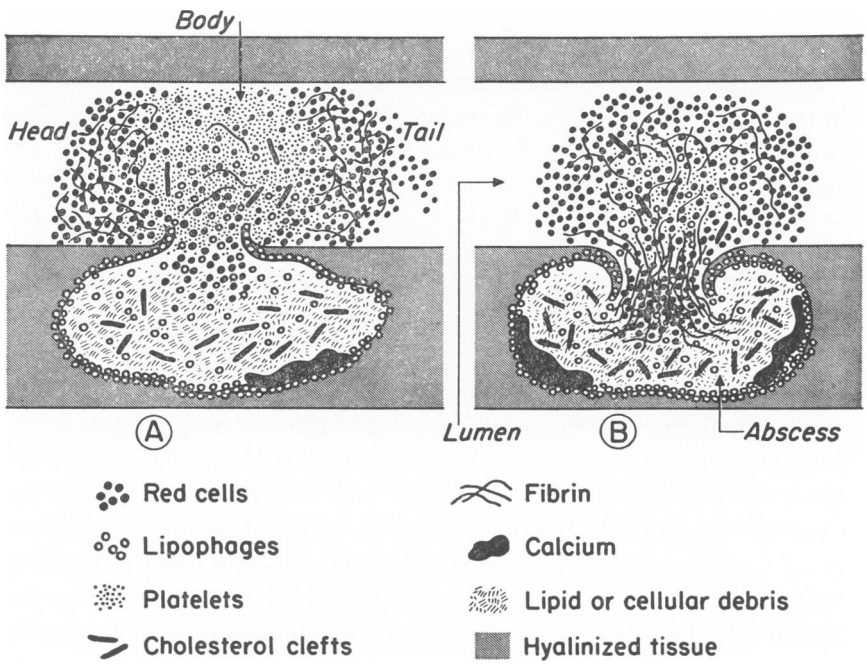
40 segments and was always due to one or more rents (i.e. fractures) in the lining of the artery between the thrombus and the atheroma. In addition to the relatively large "abscesses" in communication with the occluding thrombi, rents overlay smaller, more superficially located abscesses in 14 of the 40 specimens. Invariably these areas also were covered by layers of platelets, red cells and fibrin (Fig. 29). In the one thrombosed vessel in which a communicating rent was not observed the thrombus was old and its recanalized channels had bled and blocked forward flow.

The length of the fractures varied greatly (range, 200 to 4,700 μ) but averaged 1,935 μ in the 18 specimens suitable for such measurement. Their width varied from 50 to 500 μ but in almost all cases was considerably less than their length.

The initial direction of the rent could be determined in 36 of the 40 cases. The device used to determine this point was observation of the lumen wall in those serial sections immediately adjacent to the site of actual fractures. Here, a thinned out but intact portion of the lumen wall was observed (Figs. 3, 7, 23, 25, 30 and 32) to bulge or point toward either the atheromatous abscess or the lumen. Most fractures pointed toward the lumen and at the actual site of cleavage, the frayed ends of the fractures also pointed in the same direction (Figs. 4, 5, 24, 29 and 33, and Text-fig. 1A). Frequently also the actual entrance of abscess material into the lumen could be observed (Figs. 5, 31 and 33). Conversely, the transit of blood elements into an abscess cavity appeared (Figs. 8, 9, 26–28 and Text-fig. 1B) in those fractures pointing outward. In one segment (Fig. 10), the blood in the lumen had not only forced its way into a large cavity but had then proceeded to disrupt the opposite wall of the abscess and to infiltrate the adjacent fibrous tissue and the remainder of the neighboring tunica media and adventitia. This was indeed an example of the rare entity, coronary apoplexy.[25] It is of interest that the 29-year-old patient from whom this artery was obtained had an average blood pressure of 290/180 for many weeks prior to the occurrence of the fatal coronary lesion.

Employing these criteria, it appeared that in 26 of 36 cases suitable for such scrutiny (approximately 72 per cent) an intramural abscess had impinged progressively upon, displaced luminalward and finally destroyed the segment of the wall separating the abscess content from the blood coursing through the lumen. In the remaining 10 cases, however, the vascular lining appeared to have burst outward into an abscess cavity. Regardless of whether the initial event was extrusion of atheromatous material into the lumen or entrance of blood into the atheroma cavity, the blood in each of the 36 cases, had obviously been in contact

with the content of an atheromatous abscess. Hemorrhage was found within 25 of the 26 abscesses which had ruptured into the lumen and in all of those in which the reverse had occurred. In 34 instances the accumulation of blood was very sharply localized within that area of the abscess immediately adjacent to or surrounding the point of fracture.



TEXT-FIG. 1A. The rupture of an atheromatous abscess and the discharge of some of its debris into the lumen leading to thrombus formation is schematically illustrated. The 'body' of the thrombus is composed chiefly of platelets and cellular debris and only a few red cells and fibrin fibers. 1B. The rupture of the lumen into an abscess is shown. The thrombi following this type of rupture contain fewer massed platelets but more red cells and fibrin which frequently enter into the abscess cavity. These latter are also more homogeneous and less likely to exhibit the 3 components usually observed in thrombi occurring after rupture of an abscess into the lumen.

Regardless of whether the fracture had occurred in the direction of the lumen or the abscess cavity, the cause always appeared to be the same, namely, a prior fragmentation of that part of the hyalinized wall separating the lumen from the atheroma (Figs. 3, 7 and 23). The mural destruction was almost always observed to be preceded by or associated with its invasion by lipophages (Figs. 9, 11, 12, 30 and 32) which invaded from the abscess itself. The cells not only advanced toward the lumen but also frequently toward the tunica media and adventitia as well. In 10 of the 40 specimens, an abscess with a cellular vanguard of lipophages extended outward to cleave through the tunica media and to infiltrate in turn the tunica adventitia itself (Figs. 13 to 15). Thus the

tendency of the atheromatous abscesses to invade and destroy was not limited solely to relatively amorphous and avascular tissue but could as well involve previously intact, well-vascularized and viable components of the vessel wall.

The Thrombus in Occluded Arterial Segments

Serial sections of the 40 thrombi established the primary role of mural fragmentation with communication between atheroma and lumen blood in the pathogenesis of the thrombus. Undoubtedly the most significant evidence was the observation that the majority of thrombi (30 of 36 examined for this feature) contained isolated as well as large clusters of lipophages (Figs. 16, 34 and 35), or cholesterol clefts (Figs. 5 and 16) or large masses of seemingly intact atheromatous debris (Fig. 17) or even fragments of the ruptured wall itself (Fig. 18). The disseminated and frequently central distribution of these within the thrombi indicated tellingly that these elements must have entered into the lumen prior to and not after the thrombotic process had begun.

The structure and composition of the thrombi usually depended in great part upon whether, following fracture of the wall, the content of an atheromatous abscess first emptied into the lumen or, conversely, whether the blood in the lumen first burst into the abscess cavity. In those instances where entrance of blood into a cavity appeared to be the initial and predominant direction of fluid transit, the thrombi usually appeared to be relatively homogeneous in structure and consisted of red cells, a few atheromatous elements and some platelets, all enmeshed in fibrin strands (Text-fig. 1B). Frequently, threads of fibrin extended from the body of the thrombus to enter and fan out (Figs. 27 and 28 and Text-fig. 1B) within the abscess cavity.

These thrombi, however, in which the initial direction of transit appeared to be from the atheroma into the lumen differed rather markedly (Text-figs. 1A and 1B). The majority (24 of 26) consisted of two rather distinct portions, a 'head' and 'body', and 22 also possessed a third segment, a 'tail.' The 'head' which occupied the lumen proximal to the area of wall fracture was composed almost entirely of red cells and fibrin (Fig. 19). The 'body' was that portion of the thrombus immediately contiguous to the area of fragmentation. It consisted predominantly of a myriad of aggregated platelets (Fig. 20), scattered red cells, various cellular and acellular elements derived from the atheroma and occasional strands of fibrin. The abscess cavity itself rarely contained any fibrin. On the other hand almost always, a few red cells appeared in the cavity but were localized to its mouth (Fig. 33). The 'tail' found in most of the thrombi (Fig. 21), began at varying distances from the fracture. Its

general structure and content were similar to those observed in the proximal portion of the thrombus.

Discussion

The present study has clearly indicated that in a great majority of 40 cases of coronary thrombosis (97.5 per cent), the thrombus lay in direct communication with a pre-existing intramural atheromatous abscess. It has also been shown that such communications were accomplished by destruction of the portion of the arterial wall which separated the necrotic mass from luminal blood. The destruction was preceded by or associated with an infiltration of the vessel wall by lipid-containing macrophages extending from remnants of tissue encompassing the abscess.

Direct communication of lumen with intramural abscess is believed to have preceded and been responsible for the thrombotic process in almost every case. This was suggested by a number of observations. First, progressively more severe erosion of the lumen wall was observed in serial sections as the actual site of cleavage was approached. Secondly, the direction of the bulging fragmented ends of the ruptured wall lay either in the direction of the lumen or the abscess itself clearly indicating the flow of either atheromatous gruel or blood to effect such inclination prior to thrombosis. Fractures at the sites of cleavage, moreover, could not be artifactual because in serial sections, the previously eroded but unfragmented walls pointed or bulged in the same direction as the fragmented ends at the site of rupture. Thirdly, in the ruptures directed toward the abscess, strands of fibrin and erythrocytes were frequently observed (Figs. 8, 9, 27, 28 and Text-fig. 1B) extending from the lumen to fan out into the abscess cavity— a phenomenon indicating that breakthrough had preceded the thrombosis. Fourthly, the majority of thrombi examined (83 per cent) contained elements of atheromatous gruel or portions of the fragmented walls,— clear evidence of their entrance into the lumen by rupture of the wall necessarily prior to thrombosis. Fifthly, that portion of the thrombus adjacent to the rupture site in cases where the abscess had ruptured into the lumen consisted chiefly of platelets (Figs. 4, 5, 16, 20, 27 and 31), an orientation strongly suggesting that blood had still been flowing, hence depositing platelets, at the site of impending rupture.

An apparent priority of one of two successive events does not necessarily prove that the earlier event caused the second. It is our belief, however, that the exposure of lumen blood to an atheromatous abscess or its extruded contents was the direct cause of the thromboses observed in our specimens. We believe this because arterial tissue content is

thrombogenic [26,27] although the atheromatous debris itself is less so.[28] Secondly, in most instances platelet aggregation and maximum fibrin deposition occurred precisely at that point where lumen blood was confronted by injured, fragmented tissue. Thirdly, many smaller wall fractures besides those underlying thrombi were observed and every one of these was covered in part or completely by platelet aggregations or fibrin and erythrocytes.

In short, it would appear that contact between an atheromatous abscess with lumen blood always initiates some degree of thrombosis and it could well be that whether the thrombus becomes occlusive or merely a mural deposit depends upon the diameter of the remaining lumen [1,13,14,21] but also upon the size and possibly chemical characteristics of the atheromas.

Although rupture of an abscess in a few of our cases appeared to be preceded and facilitated by simple thinning and necrosis of the hyalinized segment of the wall separating it from the lumen, in most instances the fraying and erosion of the wall adjacent to and at the point of fracture were associated with infiltration by a myriad of lipophages. The question may be asked whether the lipophage invasion was responsible for the disintegration or whether the latter occurred first and then attracted the lipophages. An answer to this question is not easy to furnish. If necrosis of the lumen lining precedes lipophage invasion, there is a question as to what produces this necrosis. It cannot be due solely to ischemia as some authors [14,19,21,29] have maintained, because in 10 of the 40 thrombosed arteries, the tunica media (a coat wall supplied with blood) had been fragmented and traversed by the atheromatous wall abscess with its vanguard of macrophages.

It is of interest that Leary long ago described [24] the essential role of the intramural atheromatous abscess in coronary thrombosis. He too observed the debris of the mural abscess in some of the occluding thrombi and cited this observation as proof that the ruptured abscesses which communicated with thrombi were not postmortem artifacts. Other authors [30–34] have also observed a communication of an abscess with a coronary thrombus but they did not emphasize that the communication of the abscess with the lumen preceded and induced a lumen-occluding thrombus. Nor did they appreciate the fact that thrombosis did not take place unless such a communication did occur. Constantinides recently reported [18] his ability to detect a fissure or crack in the plaque on which a thrombus lay in 12 consecutive cases, but again he did not correlate such fissures with wall abscesses.

Undoubtedly the relatively minute area of fracture subjacent to a thrombus has been partly responsible for its frequent oversight in earlier

studies not employing serial sections. Thus, although the average length of the ruptures in this study was found to be approximately 1,935 μ, more than 20 per cent of them measured less than 1 mm in length. Perhaps, too, when such fractures were observed previously many investigators were disposed to regard them as postmortem artifacts. If, however, serial sections of the thrombosed segment had been examined, these fractures would have been recognized as the end result of a bulging, fraying and erosion of the wall discernible in areas adjacent to the site of rupture. Study of the entire thrombus would also have led to the recognition of atheromatous contents intimately enmeshed in the thrombus itself,— a phenomenon clearly indicating a temporal sequence of thrombogenic events.

The chief reason, however, that contact of abscess with lumen blood has not been recognized as the primary factor in coronary thrombosis has been the insistence on the part of a number of very able pathologists [15,19,21,22] that intramural hemorrhage usually initiates a thrombotic process.

In the present study, blood was found in most of the abscess cavities (Figs. 8, 27 and 33, and Text-figs. 1A and 1B), subjacent to and in direct contact with the lumen thrombus. We, however, do not believe its presence can serve as *prima facie* evidence of its origin from hemorrhage in the wall itself. Actually it is very difficult for us to understand how an abscess cavity could avoid receiving some blood from the lumen after the wall separating such a cavity from the lumen was destroyed. Certainly, in our cases the blood in abscess cavities underlying thrombi appeared to be derived from the lumen.

Summary

The arterial wall and thrombi in 40 coronary artery segments were examined by serial section. A fracture of a portion of the lumen wall allowing contact between the thrombus and the internal structures and atheromatous content of an intramural atheromatous abscess was found in 39 of the 40 cases (97.5 per cent). This fracture and the communication between lumen and atheromatous abscess preceded and were responsible for the formation of the thrombus.

Addendum

Subsequent to the submission of this article, Chapman has reported (*Arch. Path.*, 1965, 80, 256–261) that in his study of 19 thrombosed coronary vessels, the thrombus in each instance was attached to a tear in an atheromatous plaque and in contact with atheromatous debris. The dynamic role, however, of the atheromatous abscess and its lipo-

phage component in the erosion and fracture of the plaque wall were not described.

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LEGENDS FOR FIGURES

Unless otherwise indicated, photographs were prepared from sections stained with phosphotungistic acid-hematoxylin.

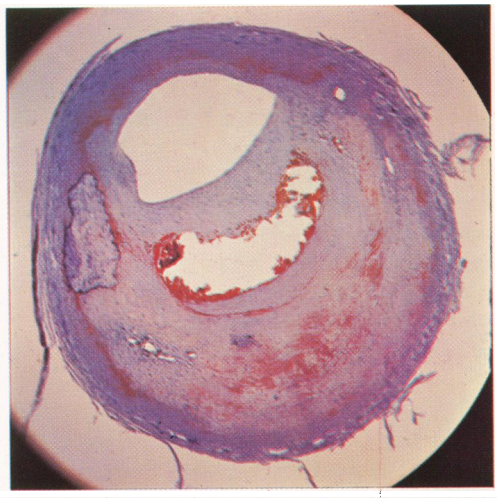
FIG. 1. Non-thrombosed portion of a left anterior descending coronary artery in a patient who died within minutes of the onset of symptoms. Exemplified are the pathologic processes which were generally encountered in the present series of arterial samples. The lumen (upper left) has been markedly narrowed by an eccentric, fibrous plaque. An area of calcification (upper right of lumen) is deeply embedded in the basal portion of the plaque. Below and slightly to the right of the lumen, there is a moderate sized area of necrosis (atheromatous abscess). Most of its pultaceous content has been lost in preparation but Sudan stained (red) macrophages still line the wall of the abscess. Small blood vessels can be seen above and to the right of and also below and to the left of the abscess. These can be traced to their source in the tunica adventitia. Despite the size of the plaque, little stainable lipid is present. Sudan IV stain. × 40.

FIG. 2. Non-thrombosed portion of a right coronary artery in a patient who died within minutes after the onset of symptoms. Illustrated is the blood supply (arrow) of a small abscess (below arrow). The blood vessels to the abscess, like the fibroblasts accompanying them, stem from the adventitia (above, center). × 65.

FIGS. 3 and 4. Thrombosed portion of a left anterior descending coronary artery in a patient who died 20 days after the onset of symptoms. The two photographs show the attenuation and rupture of the wall of an abscess. In Figure 3 the lumen (center) is completely occluded by a mass of red cells (blue-black color), fibrin and platelets. Four separate but interconnecting abscesses encircle approximately three-quarters of the lumen from which they are separated by hyalinized tissue (pink). A portion of the wall has become attenuated (above, center) and bulges toward the lumen. Figure 4 (200 μ distally) shows the rupture of the wall that had separated the abscess (upper right) from the lumen. The thrombus itself is lighter in color than it was in Figure 3 because of a greater number of platelets at this point. × 25.

FIG. 5. Portion of a thrombosed segment of the left anterior descending artery in a patient who died 90 minutes after the onset of symptoms. The rupture (between arrows) of a large abscess (upper half of artery) into the lumen (below) is clearly shown. The lipid-rich (red) content of the abscess has entered the lumen and constitutes the upper third of the thrombus occluding the lumen. The remainder or lower two-thirds of the thrombus consists chiefly of platelets although the lower outer fringe of the thrombus is composed chiefly of red cells. Many cholesterol clefts can be seen in the debris remaining in the abscess and a few can be seen also in the lipid-rich portion of the thrombus. An area of calcification (above, center) lies in contact with the abscess. Sudan IV stain. × 25.

FIG. 6. Thrombosed segment of a left anterior descending coronary artery in a patient who died 22 hours after the onset of symptoms. The rupture of an abscess (between arrows) into a very much reduced lumen is shown. The thrombus consists of platelets in its lower half (light purple color) in the vicinity of the rupture and of red blood cells and fibrin (dark blue color) in its upper half. The ruptured ends of the wall point toward the lumen. A large abscess occupies almost the entire left half of the artery. Actually the entire plaque was honeycombed with interconnecting abscesses. × 40.



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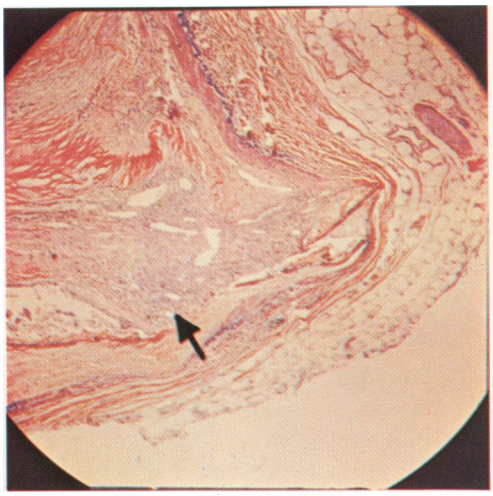

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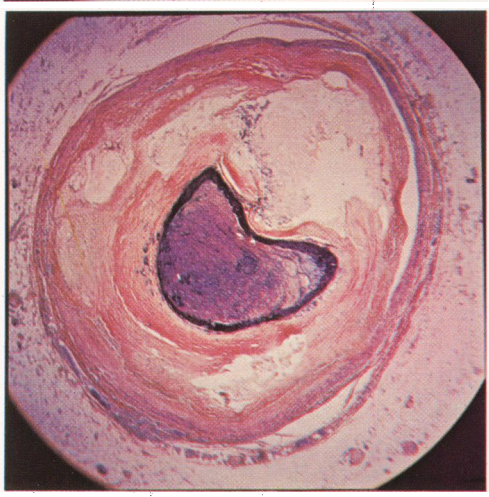

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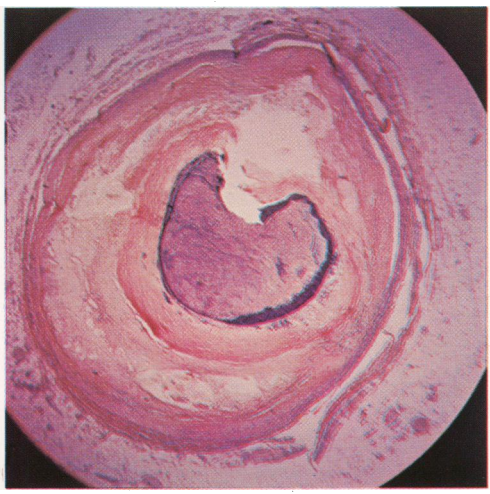

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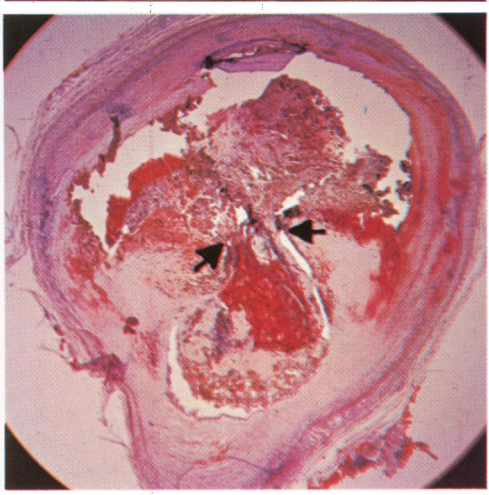

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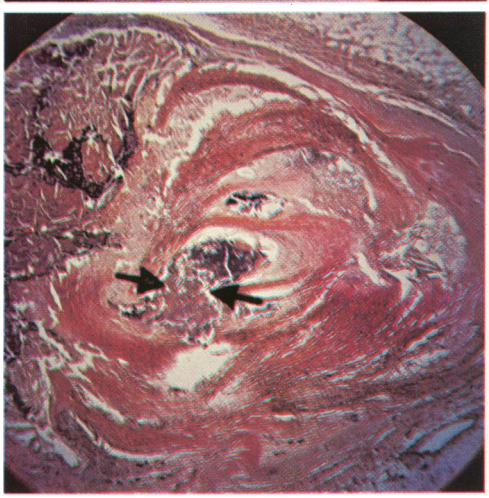

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FIGS. 7 to 9. Thrombosed segment of the coronary artery shown in Figure 2. The three photographs illustrate the attenuation and rupture of the wall toward the abscess. In Figure 7 the narrowed lumen (above, center) is separated from a large abscess lying below it by hyalinized tissue which is thinned and bulges toward the abscess at the lower central portion of the lumen. Most of the occluding thrombus was lost during preparation but a portion of it can still be seen (blue color). × 40. In Figure 8 (110 μ distally) the point of rupture is shown. There is some blood (blue-black) in the abscess but only in the immediate vicinity of the rupture. × 40. In Figure 9 the area of rupture is shown at higher magnification. The lumen is at the upper left. The ends of the fragmented wall (arrows) are directed into the abscess cavity indicating that lumen content had first ruptured into the abscess. The red cells (purple color) in the area of rupture are easily seen. × 160.

FIG. 10. Thrombosed segment of a left coronary artery in a patient who died approximately 48 hours after the onset of symptoms. Illustrated is 'coronary apoplexy.' Blood originally flowing through the narrowed lumen (A) has ruptured through the hyalinized wall below (B) to enter a large abscess (C). It again ruptures the upper part of the wall (D) enclosing the abscess to break through the media (E) and reach the adventitia (F). A long slender, red staining fragment (G) of the original wall has been pushed into the abscess cavity by the blood escaping from the lumen, thus indicating the direction of the original rupture. × 40.

FIG. 11. A section of a thrombosed segment of a right coronary artery in a patient who died less than 12 hours after the onset of symptoms. A portion of the wall separates the lumen (left) from an abscess (right). The disintegration of this wall and its invasion by lipophages is clearly shown. Clotted red cells (purple color) appear in the lumen and are also scattered in the abscess itself (above left). This wall was observed to have ruptured in a section taken 220 μ distally. × 400.

FIG. 12. Non-thrombosed segment of a left anterior descending coronary artery in a patient who died 46 hours after the onset of symptoms. The lipid content of the macrophages invading the wall just beneath the endothelium is made manifest by their retention of Sudan staining. The lumen lies above. Sudan stain. × 160.

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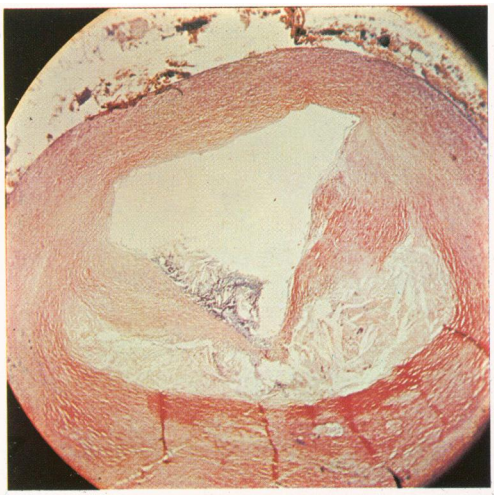

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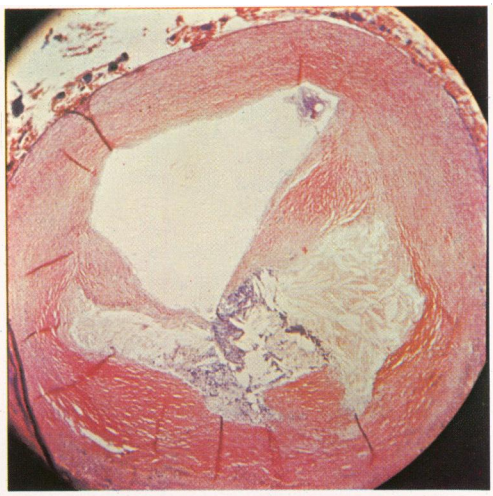

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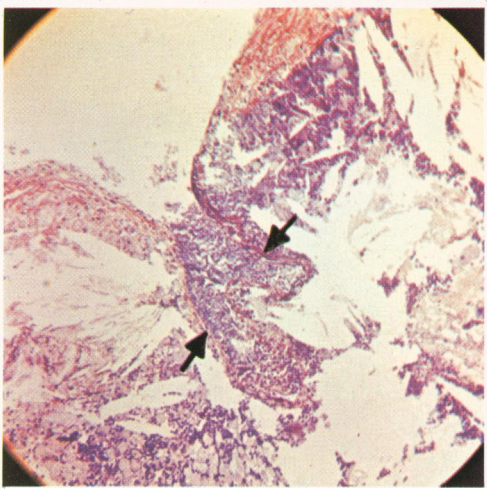

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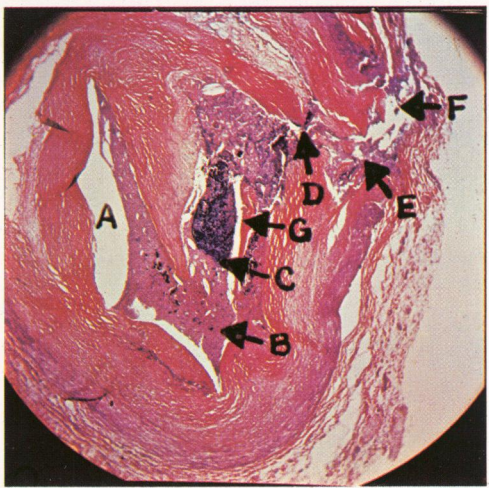

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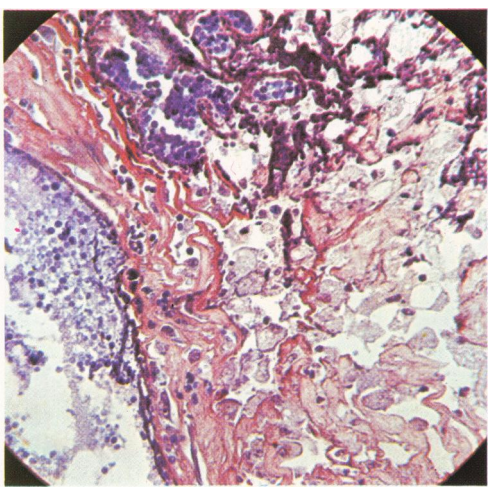

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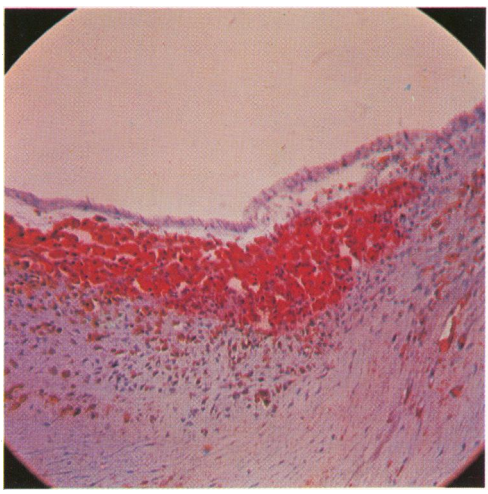


Figs. 13 to 15. Thrombosed segment of a left circumflex coronary artery in a patient who died 3 hours after the onset of symptoms. The photographs illustrate the extension of an abscess through the tunica media.

FIG. 13. A large abscess (arrow) occupies approximately one-fourth of the thickened artery, but is still surrounded by an attenuated but intact, purple staining, tunica media. × 40.

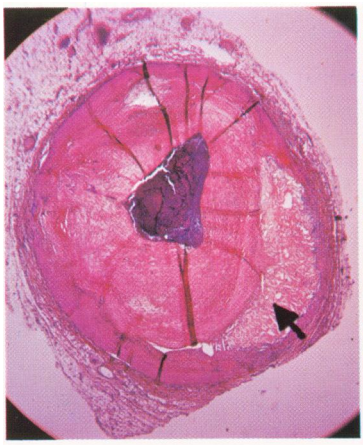
FIG. 14. (1,500 μ distally.) The abscess is observed to have penetrated the body of the tunica media (arrow). The latter has split and one portion still completely encircles the emerging abscess. × 40.

FIG. 15. (1,900 μ distally.) The abscess has penetrated completely through the tunica media (arrow) which is intact once again but is now internal to the abscess. The abscess itself now lies in the tunica adventitia. The cells forming the head or vanguard of the abscess in this breakthrough comprise a mantle of macrophages. The 'tail' of the thrombus is seen in Figure 13. × 40.

FIG. 16. Thrombosed segment of a right coronary artery in a patient who died 22 hours after the onset of symptoms. The thrombus occluding the entire lumen is composed chiefly of massed platelets (greyish white), a large, rather isolated mass of red cells (reddish-brown and at right center of thrombus) and a large number of lipid-containing macrophages (red). Cholesterol clefts are evident in the lipid-laden debris of the thrombus (left center of the thrombus). Sudan IV stain. × 25.

FIG. 17. Thrombosed segment of a right coronary artery in a patient who died 16 hours after onset of symptoms. The thrombus in the lumen consists of platelets (lilac color) in its lower two-thirds surrounding a central mass of red cells and fibrin (blue-black). The left upper third of the thrombus is composed, however, of the relatively unchanged lipid debris with cholesterol clefts usually found in an abscess. Here again the presence of this debris intermingled with red cells, fibrin and platelets indicates abscess rupture prior to thrombosis. × 25.

FIG. 18. Thrombosed segment of a right coronary artery in a patient who died 20 minutes after the onset of symptoms. The thrombus is composed chiefly of platelets (lilac color) with some blood and fibrin (black) in its upper part. At the base of the thrombus, a detached fragment of hyalinized luminal wall (bright red color) has become incorporated into the thrombus. Fragmentation and truncation are evident in the hyalinized tissue (red) originally encircling the lumen. × 25.



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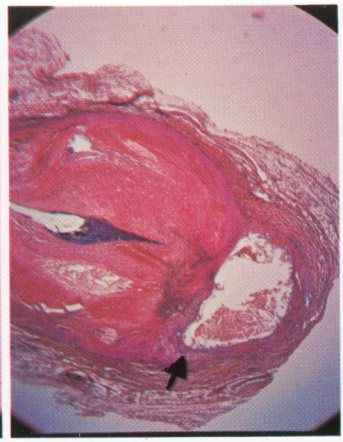

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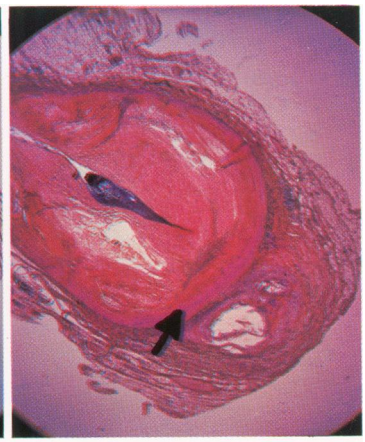

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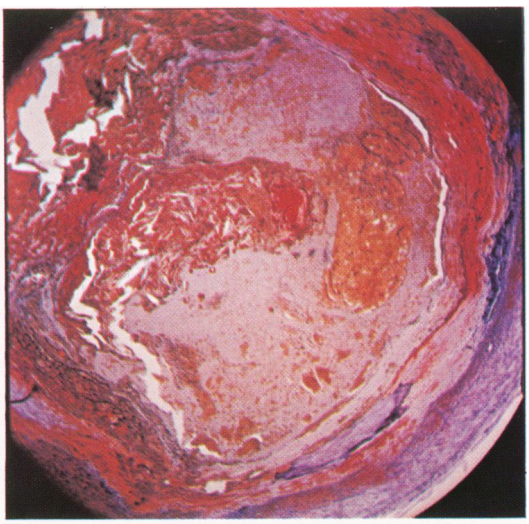

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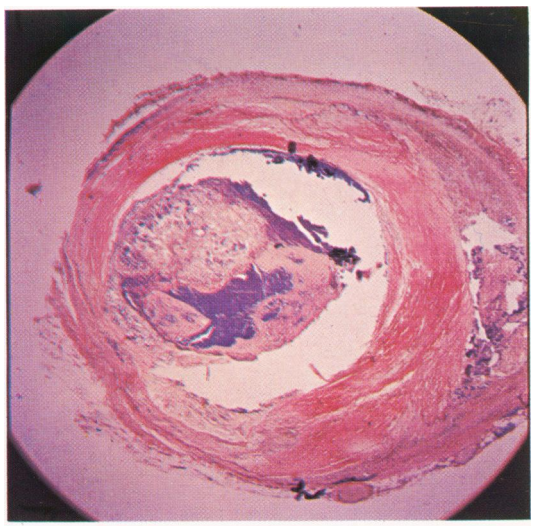

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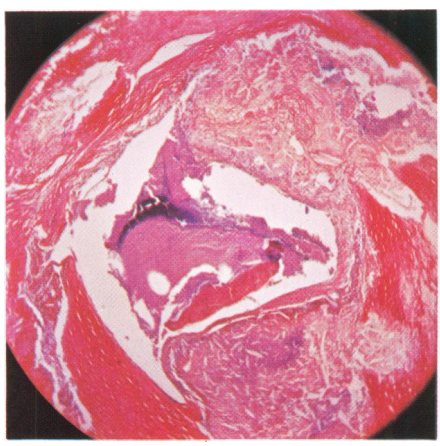

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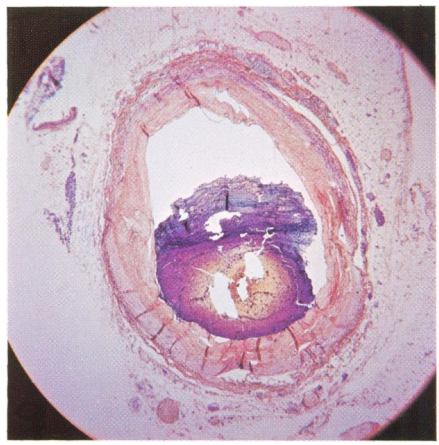
Figs. 19 to 21. Thrombosed segment of a right coronary artery in a patient who died 3 hours after the onset of symptoms. The 3 photographs illustrate the 3 parts of an occluding thrombus.

FIG. 19. The 'head' of the thrombus is composed almost completely of red cells, fibrin and serum (yellowish material in the center of thrombus). × 25.

FIG. 20. (600 μ distally.) The 'body' of the thrombus is composed chiefly of platelets (lilac colored, undifferentiated mass in lumen) although a small mass of red cells (purple-black) is embedded deep in the thrombus. The luminal wall has ruptured (below) allowing communication between the abscess and the lumen. × 25.

FIG. 21. (940 μ distally.) The 'tail' of the thrombus, like the 'head', is composed chiefly of red cells and fibrin. The 'head' of the thrombus (because of its position proximal to the narrowed portion in which the initial rupture and platelet aggregation occurred) has a greater diameter than the 'body' or the 'tail.' × 25.



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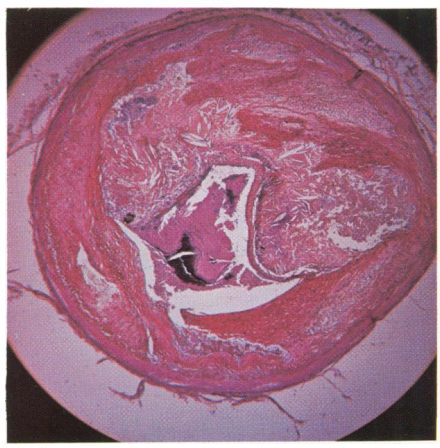

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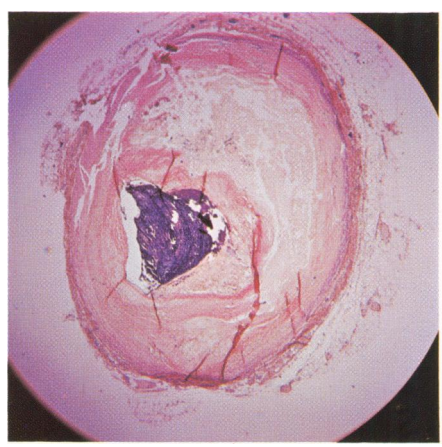

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FIG. 22. Portion of a non-thrombosed segment of a right circumflex artery in a patient who died within minutes after the onset of symptoms. Illustrated are the blood vessels supplying an abscess. These vessels lie within the angle formed by the walls of the abscess (above) and those of the encroached-upon lumen (below). Serial sections show that the vessels arise from the tunica adventitia (Fig. 2). There are cholesterol clefts in the abscess. × 65.

Figs. 23 and 24. Thrombosed segment of a right coronary artery in a patient who died 18 hours after the onset of symptoms. The two photographs illustrate the sequence of necrosis, bulging and rupture of the hyalinized wall separating an abscess from the lumen. × 40.

FIG. 23. The lumen (center) is separated from an encircling abscess by a markedly attenuated hyalinized wall which exhibits necrosis in at least two areas (arrows). × 40.

FIG. 24. (75 μ distally.) The rupture shown occurred in the upper one of the two necrotic areas demonstrated in Figure 23. The direction of the rupture as shown by the torn wall fragments was probably toward the lumen and explains the presence of abscess debris and cholesterol clefts in the thrombus. × 40.

Figs. 25 and 26. Thrombosed segment of a right coronary artery in a patient who died approximately 120 minutes after the onset of symptoms. The two photographs of the lumen and a portion of the surrounding abscess illustrate the attenuation and rupture of the wall into the abscess cavity.

FIG. 25. The lumen contains a portion of the original thrombus which remained after fixation. The attenuation and bulging of the wall can be seen at the upper right. × 65.

FIG. 26. (80 μ distally.) The rupture in the same area of the lumen and the passage of red cells into the abscess cavity are apparent. Such a passage could only have occurred prior to thrombosis. × 65.

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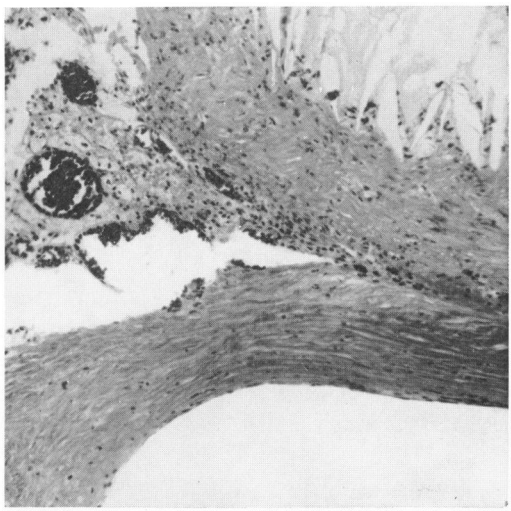

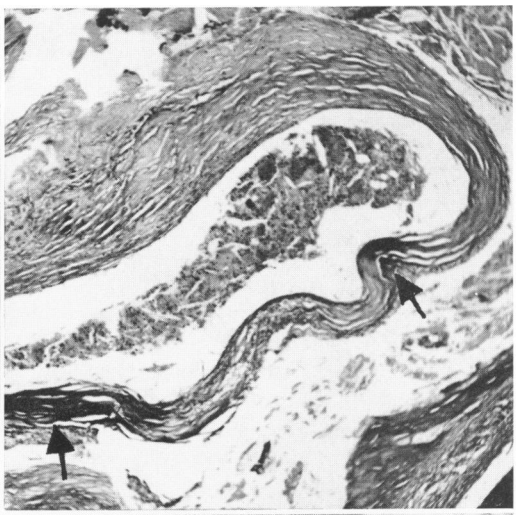

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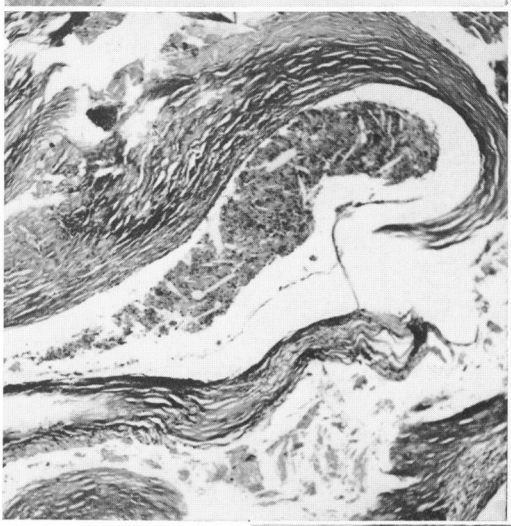

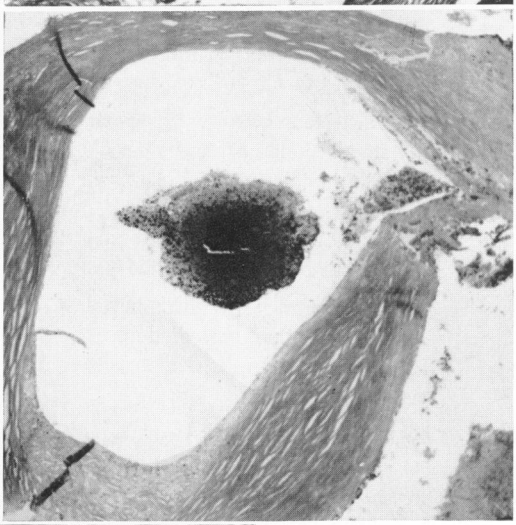

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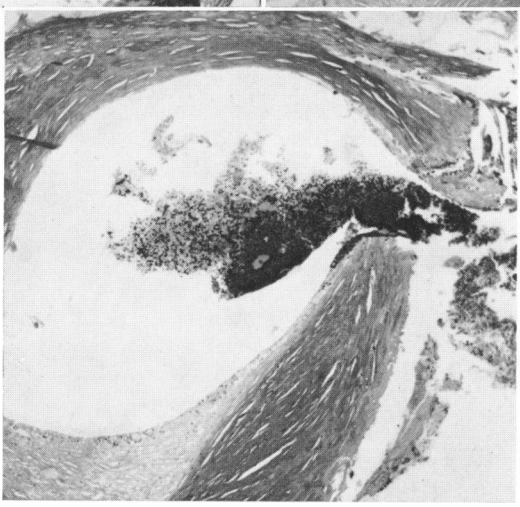

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Figs. 27 and 28. Thrombosed segment of the same right circumflex coronary artery shown in Figure 22. The two photographs show the rupture of the wall into the abscess.

FIG. 27. The thrombosed lumen (below and to right of center) is markedly narrowed and lies between two huge abscesses which completely encircle it. At the upper part of the lumen, rupture of the hyalinized wall (arrow) has occurred and blood can be seen entering the abscess cavity. Blood in the abscess is localized, however, to the rupture site. The major portion of the thrombus consists of platelets (greyish white). × 25.

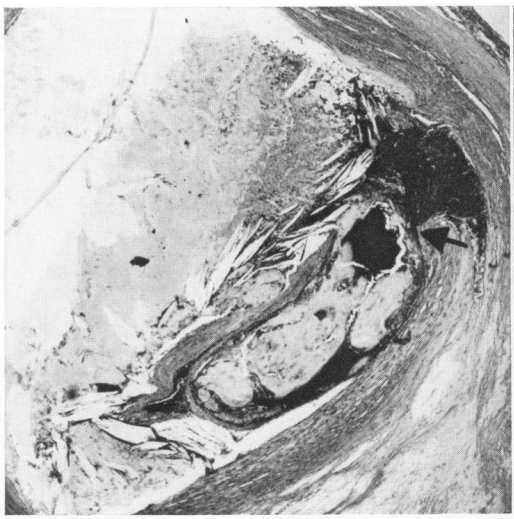
FIG. 28. The area of rupture is shown at greater magnification (× 160). The deflection of the wall fragment (arrow) and the fanning out of the fibrin strands from the rupture into the abscess indicate that the direction of the rupture was from lumen into the abscess.

FIG. 29. Non-thrombosed segment of a right coronary artery in a patient who died several hours after the onset of symptoms. The ruptured abscess is quite small. The inclination of the fragments indicates that the abscess ruptured into the lumen. The surface deposit of fused platelets just to the left of rupture and that of red cells to right may be noted. A few red cells (black round masses) appear in the abscess cavity. × 160.

Figs. 30 and 31. Thrombosed segment of a left anterior descending coronary artery of a patient who died approximately 30 minutes after the onset of symptoms. The two photographs demonstrate the cellular invasion of the vessel wall and its rupture.

FIG. 30. A portion of the bulging wall separates the thrombus (lower right) from the abscess cavity (clear area on left). Although the wall is still intact, its original dense hyaline structure has been invaded (upper, right) by lipophages lining the abscess cavity. Most of the thrombus is composed of platelets (lower, right). × 160.

FIG. 31. (300 μ distally.) One of several areas of rupture is shown (between arrows). The disintegrated, macrophage invaded fractured ends of the wall (arrows) are well shown here. There is a heavy preponderance of fused platelets in the thrombus (lower, right). × 160.



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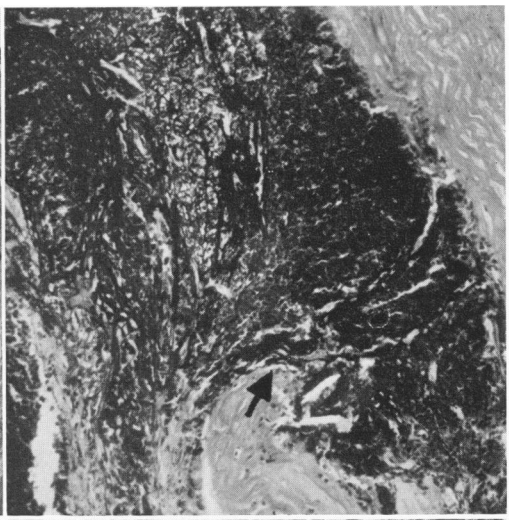

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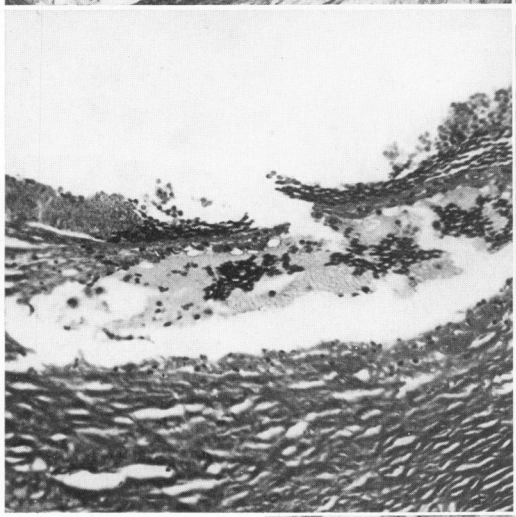

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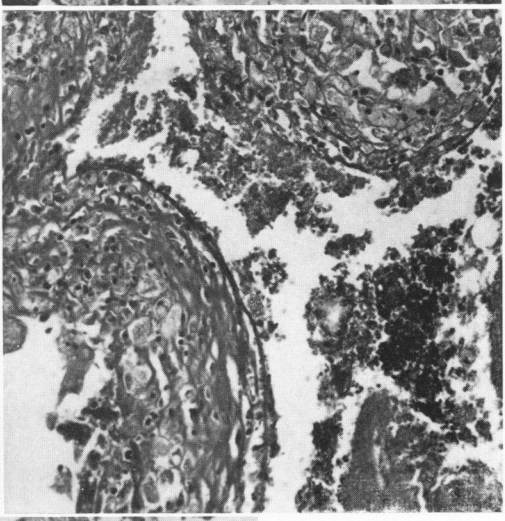

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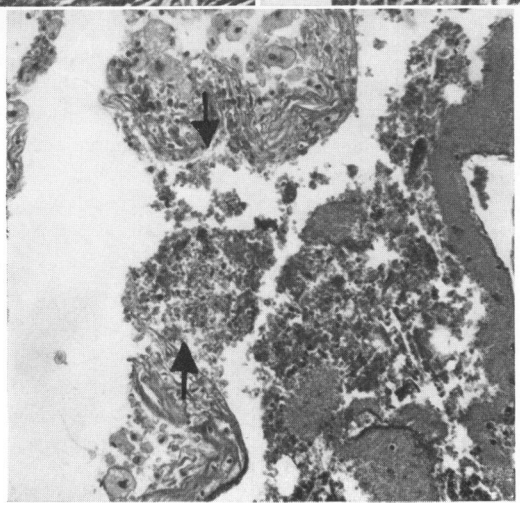

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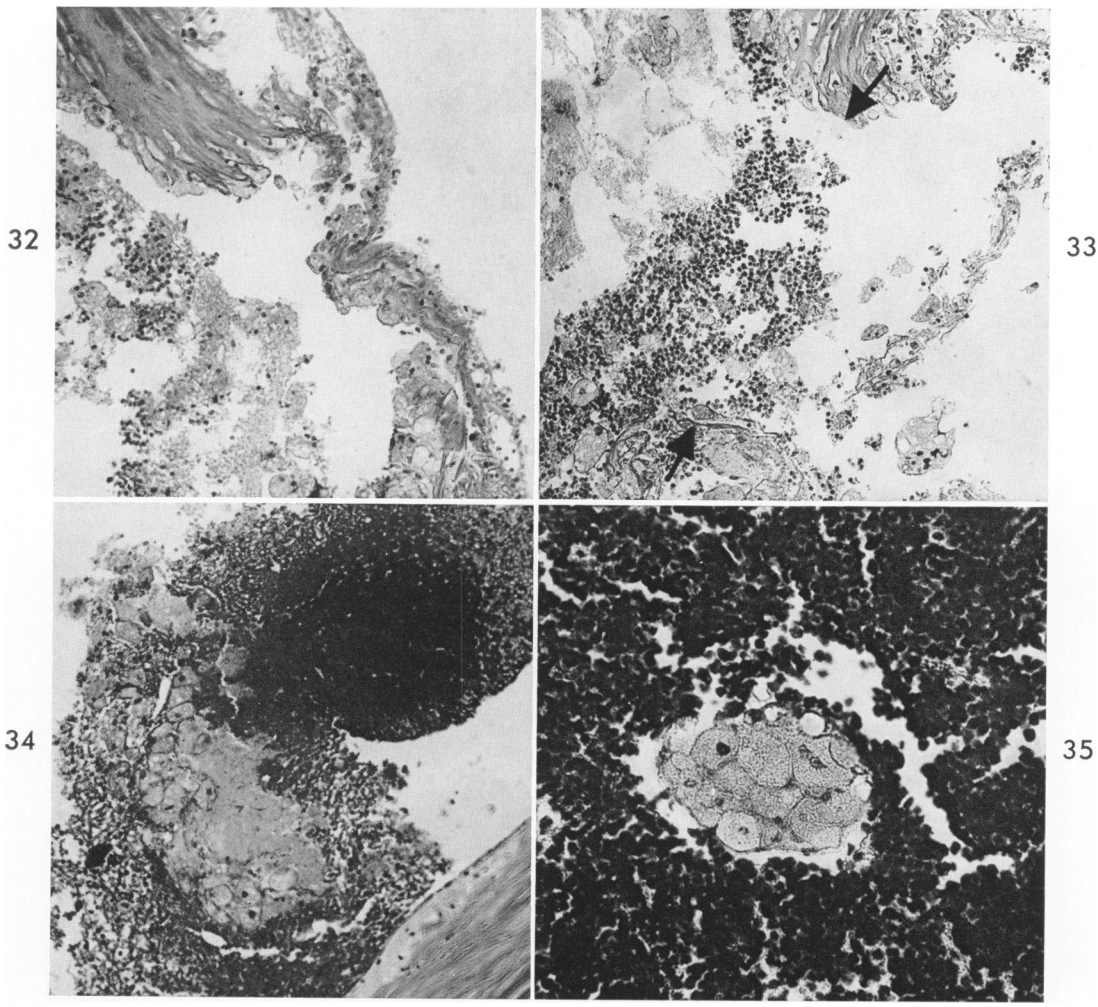

Figs. 32 and 33. Thrombosed segment of a left anterior descending coronary artery in a patient who died less than 12 hours after the onset of symptoms. The two photographs show another example of disintegration and rupture of the luminal wall.

FIG. 32. A thinned wall separates the lumen (right) from an abscess containing debris, red cells and lipophages. The latter have replaced almost all of the hyalinized fibers originally comprising the attenuated bulging wall. × 160.

FIG. 33. (160 μ distally.) A point of rupture is shown (between arrows). The upper fragment (upper arrow) exhibits mostly hyalinized tissue but the lower fragment (lower arrow) is completely disintegrated and abounds in lipophages. The direction in which the upper fragment points suggests that the abscess had ruptured into the lumen. There is a concentration of red cells (small black dots) in the abscess at the point of rupture. × 160.

FIG. 34. A thrombus in the right coronary artery of a patient who died 10 minutes after the onset of symptoms. The thrombus is composed chiefly of red cells and fibrin but a goodly number of lipophages with amorphous masses of platelets are also present in the lower half of the thrombus. × 160.

FIG. 35. Another section of the thrombus in Figure 34. A collection of lipophages is deeply embedded in the red cell-fibrin mass of the thrombus. Their presence indicates, of course, that a rupture of an abscess has occurred prior to the thrombosis. × 400.