

AN INFLAMMATORY BASIS FOR CORONARY THROMBOSIS *

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Occlusion of a coronary artery is almost always due to a thrombus or an embolus. Of the twenty-three cases of occlusion reported by Wolff and White¹ nineteen were due to thrombosis and four to embolism. The usual sources of emboli were either a mural thrombus of the left ventricle or a vegetative endocarditis. Thrombosis never occurs in a healthy vessel, while emboli may occlude normal coronary arteries. In Hamman's² review of the relative frequency of thrombosis and embolism, he reports that Longcope had sixteen cases of thrombosis and one occlusion by embolus; that Faulkner, Marble and White had twenty-five cases of thrombosis showing arteriosclerosis and one vegetative endocarditis with embolism; that LeCount had twenty-nine cases of thrombosis and one of endocarditis with embolism.

Wolff and White state that "the most commonly involved vessel is the anterior descending branch of the left coronary artery, but any of the other branches may be the seat of the occlusion." Of their nineteen cases of thrombosis the left coronary was involved in thirteen, the right in four, both in one case; and the remaining one was an unusual case with the occlusion at the root of the aorta. Wearn³ reports that sixteen out of his nineteen cases showed the occlusion in the anterior descending branch of the left coronary, one in the posterior descending branch, and one in the posterior circumflex branch of the left coronary. In the review by Hamman, referred to above, he reports that of thirty cases the anterior descending branch of the left coronary artery was occluded in twenty-two cases, the orifice in two and the left circumflex in one case, while the right coronary artery was involved in five cases. Of course not all of these cases showed thrombosis. Twenty-five showed arteriosclerosis, four syphilitic aortitis, and one an embolus. We see from these records that occlusion occurs most frequently in

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the anterior descending branch of the left coronary artery and that the occlusion is almost always due to thrombosis.

In practically every case of coronary thrombosis described there has been generalized arteriosclerosis or at least sclerosis of the coronary arteries. However, in two of Herrick's ⁴ cases the only significant vascular sclerosis was in the coronary arteries. Riesman ⁵ states that the etiology of coronary thrombosis coincides with that of coronary sclerosis. According to Wearn, in addition to the coronary arteries which were markedly sclerosed in every case, there was sclerosis of the aorta varying from mere fatty plaques to extensive atheromatous ulcerations with calcification. Hamman found that the chief cause of occlusion was arteriosclerosis and the final closure was usually due to thrombosis. He concluded that arteriosclerosis alone would cause such gradual obstruction that a compensating collateral circulation would develop so as to prevent alarming symptoms. But when the vessel has become markedly diseased, even before the inner walls have approximated, thrombosis usually occurs to occlude the vessel abruptly. Gordinier ⁶ also mentions the atheromatous changes in the coronary arteries associated with coronary occlusion. Wolf and White state that "the coronary arteries in all cases of thrombosis are sclerosed, and usually narrowed." They agree with Hamman as regards the arteriosclerosis and narrowing of the lumen, and add that "an exceptional case may show only very slight fibrotic changes, but apparently the injured intima in such instances is sufficient to allow thrombosis to occur." Willius ⁷ says that patients dying of coronary thrombosis always show arteriosclerosis of the coronaries. He adds that the aorta is also the seat of disease, consisting of sclerosis, atheroma and ulceration.

The thrombus usually forms at a point where the sclerotic changes have caused considerable narrowing of the lumen. This point is usually at a variable distance from the orifice but is not far from the bifurcation of the descending branch of the left coronary. In fifteen out of Wearn's sixteen cases the thrombus was situated on the site of a contracture in the lumen due to an atheromatous change in the vessel wall. The thrombus was not found in one of his cases but the lumen of the artery was practically closed at one point by an atheromatous thickening. One of Paullin's ⁸ cases showed thrombosis in the anterior descending branch of the left coronary and

another in the posterior circumflex of the left coronary. The thrombi formed over the calcareous plaques caused infarcts near the tip of the left ventricle and the posterior part of the left ventricle, respectively. The occlusion by a coronary thrombus usually occurs at only one point but more than one vessel may be affected.

It appears that in most cases of coronary thrombosis there is an underlying arteriosclerosis forming the basic lesion upon which the thrombus is formed. Little attention has been paid to the immediate changes which precipitate the deposition of thrombus. It is evident that a coronary artery may remain sclerosed for years without thrombosis and there must be some mechanism which eventually incites the deposit of platelets and fibrin.

This phase of the question has been considered, especially in the two cases to be described, in which the mechanism is clearly in evidence. An arteriosclerotic plaque may lead to sudden thrombosis whether it be situated in the aorta or in a coronary artery by reason of the onset of an acute inflammatory change within the plaque. The cause of the acute inflammation which may occur in atheromata is obscure, but the following cases suggest vascular injury about the atheroma, possibly from circulating toxic material derived from an extensive infection, as one agency in its production.

The outpouring of exudate into an atheromatous plaque distends it with serum, fibrin, red blood cells and white corpuscles. In the two cases studied here such an exudate and hemorrhage were very abundant, and they appear to have been superimposed upon some change, vascular or otherwise, which took place within the atheromatous areas not only in the coronary arteries but also in the aorta. Secondary to the inflammation and the distension of the sclerotic patches the fresh thrombus was deposited, effecting in the case of the coronary vessels immediate and complete occlusion.

CASE I. The first case is a white housewife, aged 65 years who entered the hospital February 27, 1927 with signs of consolidation and fibrinous pleurisy of the lower right pulmonary lobe. The onset of this condition dated back two weeks before admission when the patient had a cold and cough, followed by shortness of breath, a tight feeling in her chest and some pain.

The course was relatively uneventful until March 3 when she complained of a severe pain in the chest extending across the upper anterior portion and into the right axilla.

Four days after admission the physical signs of a non-productive cough, a prolonged expiration with a grunt in association with rales, dullness in the right chest, suppressed breath sounds and a dry friction rub in the right axilla,

were not definitely changed; but the patient appeared more acutely ill. She vomited once. The leukocyte count rose from 9,000 to 11,000. The temperature which had ranged from 99° F. to 103° F. fell to normal during the evening of March 3; and was 98.2° F. at midnight, where it remained.

The following morning at 8.30 the patient appeared to be in pain but was breathing quietly. While she was under observation, her facial expression showed anxiety and suddenly became fixed, drawn and still. There was no gasping and no struggle. Respiration ceased and her pulse and heart beat were imperceptible.

The anatomic diagnoses are: thrombosis, coronary, left descending; atheromatous degeneration of coronary arteries; acute inflammation, atheromatous areas; necrosis, myocardial, acute; bronchopneumonia, acute, suppurative; hydrothorax, right; acute passive congestion, liver; passive congestion, kidneys, spleen, adrenals and mesentery.

Pathologic Findings: Sections through the descending branch of the left coronary show a large atheromatous plaque which has pushed the thickened intima far out into the lumen of the vessel. Within this atheromatous area there are numerous cholesterol crystal clefts which take various shapes, and some of them are actually pulled apart. There is an abundant content of serum within the plaque which has caused a swelling of the entire area with a pushing out of the intima, increasing the stenosis of the lumen. There are occasional leukocytes scattered through the atheroma and also some about the margin of the plaque. About the intimal and the lateral margins of this atheromatous plaque there are numerous small blood vessels, apparently branches of the vasa vasorum, grown about its margins. Large amounts of fibrin and numerous red blood cells are deposited all about these small vessels. This hemorrhage serves further to elevate the intima and thereby obliterate the lumen still more. The endothelial surface is irregularly roughened from injury, and a fresh thrombus is deposited upon it at the site of greatest obstruction. This completes the obstruction of the already narrowed lumen.

CASE 2. The second case is a white woman, aged 60 years, who entered the hospital with a fairly typical history of gall-bladder disease. She came back later with no improvement of her previous condition. Her blood pressure was systolic 170 and diastolic 72. The leukocyte count was 16,000. She was very jaundiced and this increased along with a rise in temperature. The abdomen became very rigid and about the same time the patient passed a large stone 3 cm. in diameter by rectum. She was operated upon the following morning.

The gall-bladder had perforated into the duodenum. Following the operation for removal of the gall-bladder she apparently reacted well. The temperature rose to 102° F. The wound drained a brownish fluid. At four o'clock in the morning on the ninth day after the operation the patient died. The type of death was not known but it was thought to have been very sudden and peaceful.

The anatomic diagnoses are: thrombosis, coronary, left descending; atheromatous degeneration of coronary arteries and aorta; acute inflammation, atheromatous areas; cholecystoduodenal fistula; peritonitis, acute suppurative, encapsulated; splenitis, toxic; passive congestion, liver, lungs, mesentery and intestines.

Pathologic Findings: The intima of the descending branch of the left coronary artery is irregularly thickened and a large atheromatous plaque pushes the superficial layers of the intima out into the lumen. There are numerous cholesterol crystal clefts within the plaque. There is a large amount of serum present which has caused great swelling and an increase in the size of the plaque with a pushing out of the intima, further obliterating the lumen. Within this edematous plaque about the cholesterol crystals there have accumulated numerous cells, many of which are polymorphonuclear leukocytes. This area is softened due to partial solution of the plaque. About the outer margins of the atheroma there are some small blood vessels with hemorrhage and fibrin deposited all about them. The endothelial surface is irregularly roughened due to some injury and a fresh thrombus is attached to the vessel wall. This thrombus completely obstructs the lumen which has already been narrowed.

Within the intima of the aorta there are large atheromatous plaques which cause the intima to stand out in an irregular manner. There are many cholesterol crystal clefts about which are many polymorphonuclear leukocytes and large mononuclear leukocytes, and a great deal of serum which has caused a swelling of the entire area. This raises the superficial layers of the intima. About the outer margins of the atheromatous plaques there are some small vasa vasorum around which are hemorrhage and fibrin. This hemorrhage and the deposition of fibrin serve to increase the volume of the atheromatous area and to extend the superficial layers of the intima still farther out into the lumen. The endothelial surface is irregularly roughened and a fresh thrombus is attached in places to the vessel wall.

DISCUSSION

The acute changes which have taken place in the above described arteries leading to thrombosis are all superimposed upon a pre-existing arteriosclerosis. They have been found in the aorta and in the coronary vessels. The recent changes have been studied as they have occurred in two cases of coronary thrombosis, in one of which they were present also in the aorta.

The large atheromatous plaques form within the intima producing an irregular thickening which pushes out the superficial layers of the intima into the lumen of the vessel and thereby reduces its size. Superimposed upon these atheromatous areas are acute inflammatory changes. The plaques show the typical clefts that have been left by the cholesterol crystals which have been dissolved. About these irregular clefts serum is present in large quantities and this acute exudation has brought about a marked increase in the volume of the plaques. The increase of the volume in the atheromatous areas serves to extend the superficial layer of the intima still farther out into the lumen. In addition to the serous effusion there has been an exudation of polymorphonuclear leukocytes and large mononuclear leukocytes about the crystal clefts and an acceleration of the process of necrosis and softening. In association with the older sclerotic process numerous small vasa vasorum have grown in about the margins of the atheromatous plaques to supply the damaged wall of the vessel. There are large depositions of fibrin and extensive hemorrhages about these small vessels which indicate some injury to their walls. These areas of hemorrhage and fibrinous exudate begin about the small blood vessels and extend in toward the centers of the plaques and even out under the elevated intima. The volume of the plaques is thereby increased and the intima is raised farther and pushed out into the lumen. The acute inflammation and hemorrhage about the atheromatous areas are probably of very short duration.

The atheromatous plaque with its acute exudate and resulting softening, together with the hemorrhages about the outer margins, causes a great outpushing of the superficial layers of the intima into the lumen. The endothelial surface of the vessel becomes injured due to the various changes going on underneath it or to changes due to the circulating blood passing over the distended and irregular

intimal surface as it stands out in the lumen of the vessel. Upon this injured endothelial surface a fresh thrombus forms, which in the case of the coronary arteries further obliterates the lumen of the vessel or causes complete obstruction.

In both the cases described above there was an acute infection; in the one, an acute bronchopneumonia, in the other a suppurative localized peritonitis. The association of such infections with the acute degenerative and inflammatory process going on in the sclerotic vessels suggests a causal relationship. Infection has long been thought of as a possible etiologic factor in arteriosclerosis for one so frequently finds acutely developed fatty patches in the intima associated with various infectious diseases. That infections of various kinds are operative in acutely advancing and extending arteriosclerotic lesions, already existent but probably quiescent, is equally probable.

These two cases clearly demonstrate the fact, to which we have not found reference in the literature, that an arteriosclerotic plaque may suddenly undergo an acute degeneration associated with inflammation and that thrombosis may be the result. Such an exacerbation of an old arteriosclerosis may be general, that is, it may involve all the arteries affected, and in the case of the coronaries may lead to sudden death from an occluding thrombus.

SUMMARY AND CONCLUSIONS

1. Two cases of thrombosis of the left coronary artery are reported.
2. An acute inflammation of the atheromatous plaques appears to have been the immediate cause of the deposition of thrombus.
3. An extensive suppurative process in a person with arteriosclerosis may cause an acute exacerbation of the vascular lesions wherever they are situated, and in the case of the coronaries may lead to a fatal thrombosis.

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DESCRIPTION OF PLATES

PLATE 41

- FIG. 1. Coronary artery of Case 1. The atheromatous plaque is softened and partially liquefied. The dark areas are composed of fibrin and red blood corpuscles. There is a fresh thrombus attached to the wall of the vessel. $\times 20$.
- FIG. 2. Coronary artery of Case 2. The atheromatous plaque is softened and degenerated. The small black dots scattered throughout the plaque are polymorphonuclear leukocytes. The single irregular dark area near the margin is composed of fibrin and red blood cells. There is a fresh thrombus attached to the intimal wall of the vessel. $\times 20$.



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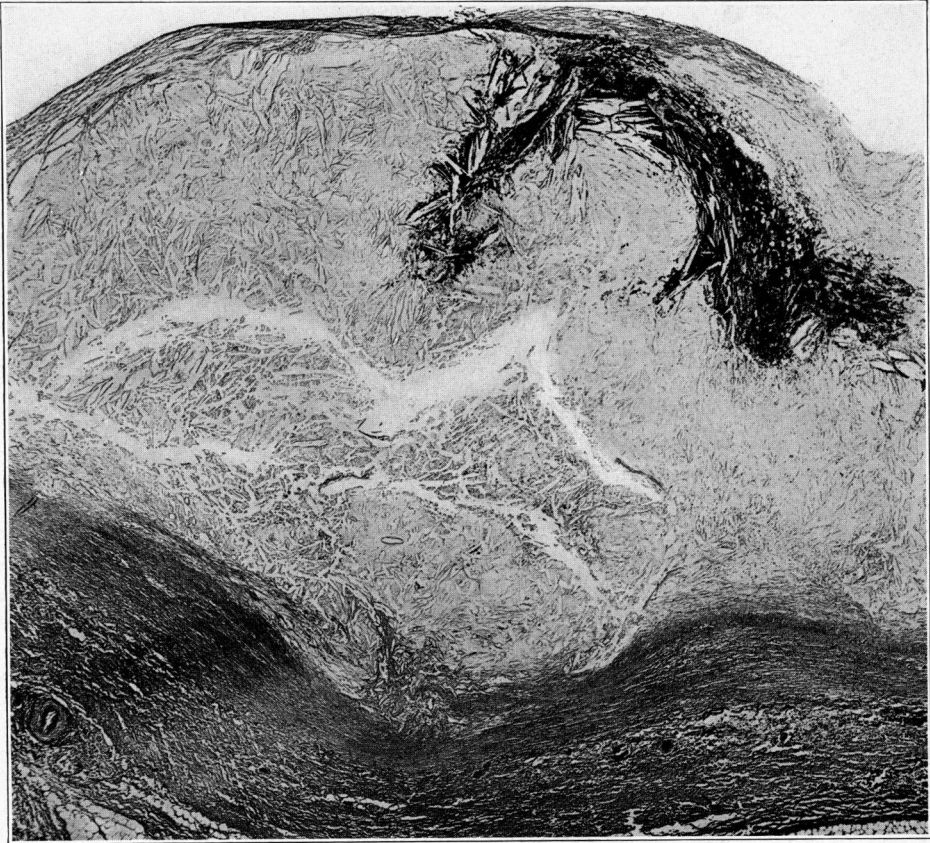
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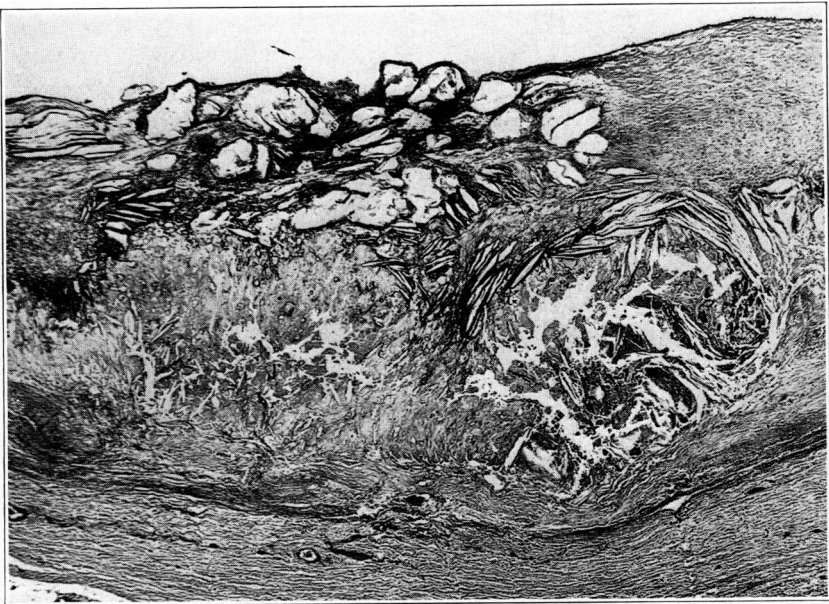
PLATE 42

FIG. 3. Section of aorta of Case 2. The large atheromatous plaque is softened. The dark areas are composed of fibrin, red blood cells and polymorphonuclear leukocytes. $\times 20$.

FIG. 4. Another section of aorta of Case 2. The atheromatous plaque is softened and almost dissolved. The numerous small dots are polymorphonuclear leukocytes scattered throughout. The darker irregular areas are fibrin and red blood cells. $\times 20$.



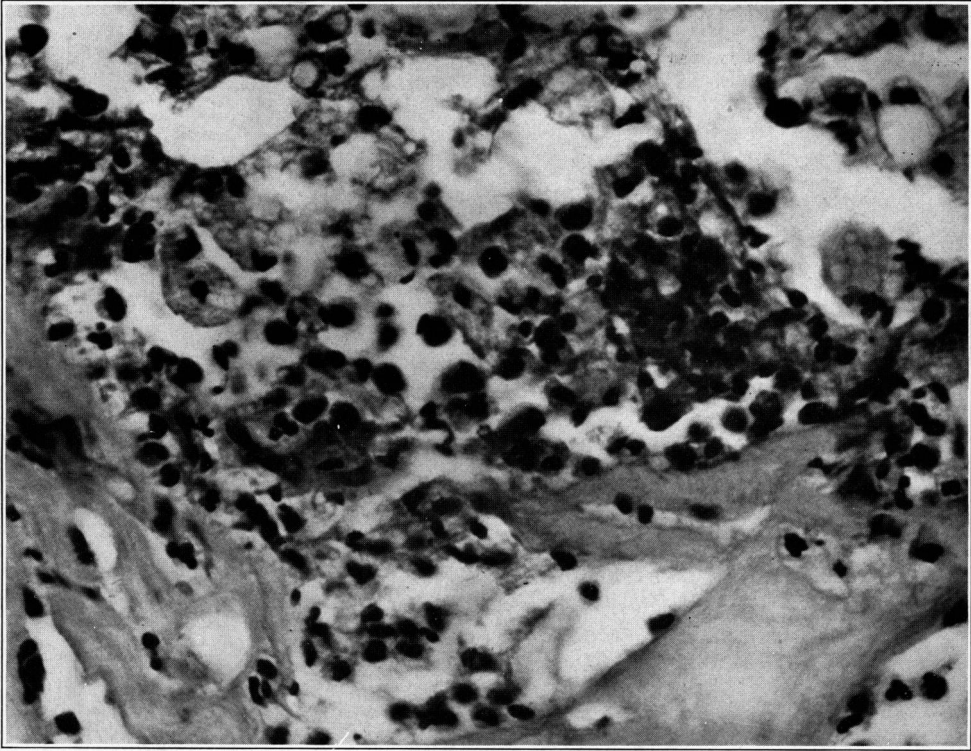
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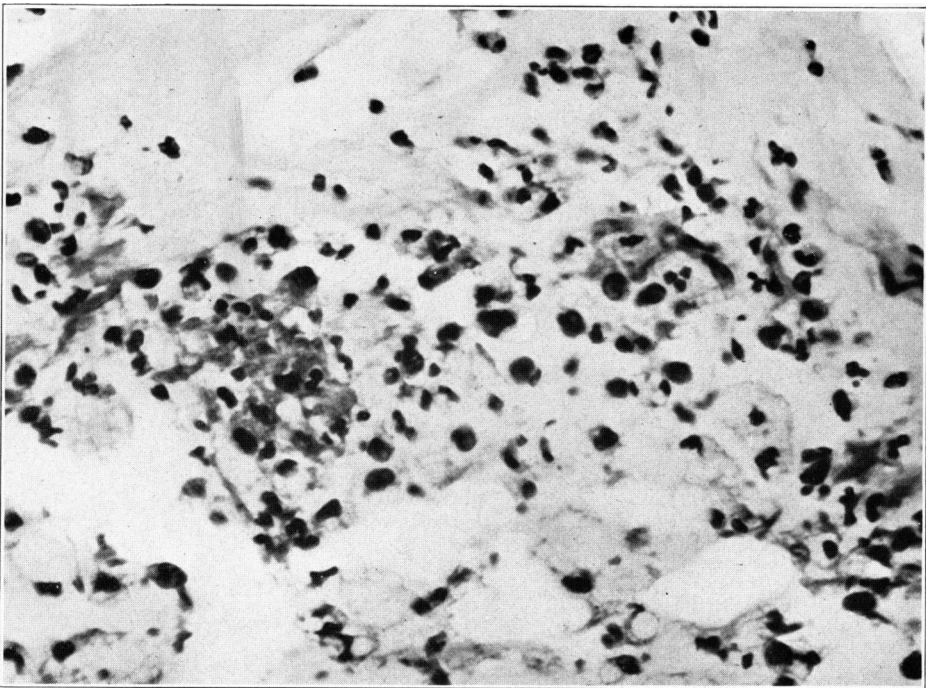
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PLATE 43

- FIG. 5. A high power view of an atheromatous plaque in a coronary artery of Case 2. The dark cells are all polymorphonuclear leukocytes. $\times 800$.
- FIG. 6. A high power view of an atheromatous plaque of the aorta of Case 2. Shows the numerous polymorphonuclear leukocytes scattered throughout in an area of softening. $\times 800$.



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