FOCAL MYOCYTOLYSIS OF THE HEART *

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In this communication we wish to focus attention on a miliary lesion of the myocardium not hitherto emphasized and commonly seen in coronary heart disease. We have characterized the lesion as focal myocytolysis. Others have described it under various designations such as acute miliary infarction,[1] focal necrotizing myocarditis without interstitial infiltration,[2] and sarcolytic myocardosis.[3]

Focal myocytolysis as it appears at the borders of cardiac infarcts was appreciated as early as 1904 by Smith,[4] but seemingly has since been forgotten. It has been described also in various noncoronary cardiac conditions.[1,2,5-9] Focal myocytolysis of the heart has been noted in several diseases not essentially cardiac.[3,10-12] It has been produced experimentally in a variety of animals.[13-16] In spite of its rather common occurrence, its morphologic and functional significance has not been appreciated generally.

In speed of evolution and histologic details, focal myocytolysis is intermediate between the reversible degenerations of the myocardium and the irreversible coagulation necrosis of an infarct. The lesion is closely similar to, and probably has been confused with, some forms of infarction. Hence, it is necessary first to delineate our concept of infarction in the heart.

General Characteristics of Cardiac Infarct

Cardiac infarct comprises three phases: necrosis, reactive exudation, and repair. By standard morphologic criteria, an infarct does not become demonstrable, grossly or histologically, for 12 to 24 hours after its *clinical* onset.

Necrosis involves not only the muscular syncytium but also the cardiac stroma. With the death of the muscle, its fibers at first increase, and later diminish, in diameter. The diminution is accompanied by smudginess, blurring of striations, increased eosinophilia, and karyolysis of the muscle nuclei. Necrosis of the stroma is shown by

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fragmentation and granularity of its reticular fibrils, blurring and altered staining qualities of its collagen, and karyolysis of its nuclei. Lysis of this necrotic tissue starts early in the periphery of the infarct and continues in a centripetal direction throughout the later phases. Acute exudative phenomena develop, with polymorphonuclear leukocytes as the most conspicuous single element. These cells are soon replaced by subacute and chronic inflammatory cells. Repair, in the form of granulation tissue, is discernible early and, with progressive fibrosis, becomes increasingly conspicuous. Healing, i.e., complete fibrous substitution, varies with the size of the infarct and, in the case of very large ones, requires many months.

Reactive exudation and repair are vital processes and thus can originate only from a viable stroma. In larger infarcts the supportive stromal structures of the heart always become necrotic. Therefore, reactive exudation and repair can manifest themselves only about the periphery of such infarcts as zonal and marginal phenomena. Repair proceeds, of necessity, in a centripetal direction.

Special Characteristics of Small and Miliary Infarcts

An important morphologic variation is introduced when the cardiac infarct is small. The basic phenomena of necrosis, lysis of necrotic tissue, reactive exudation and repair, as noted, remain identical, but they are completed in a shorter time. In small infarcts the early polymorphonuclear leukocytic infiltration may appear either zonally about the periphery or diffusely throughout the infarct. Polymorphonuclear leukocytes can advance from the viable marginal stroma only for a limited distance. Consequently, an infarct with a diameter of less than twice this distance will be diffusely infiltrated; one larger than that will not.

Apart from differences of size, smaller infarcts may differ in one other significant detail from larger ones inasmuch as their stroma does not necessarily die. If the stroma remains viable, such an infarct lacks the marginal zoning of reactive exudation and repair which are so characteristic of large infarcts. Instead, reactive exudation and repair are manifest *throughout* the small infarct. The necrotic muscular syncytium is the only element to be removed. Repair then proceeds largely by stromal collapse and stromal condensation and only slightly by fibroblastic proliferation. This detail of stromal survival of the miliary infarct sharply illustrates the differential sensitivity of stroma and muscle to the same degree of metabolic imbalance.

Characteristics of Focal Myocytolysis of the Heart

The lesion of focal myocytolysis, usually not larger than 1500 μ, closely resembles a miliary infarct without stromal necrosis, but differs in some essential respects. In this form of myolysis the muscle fibers disintegrate within a small and discrete territory. Their myofibrils seem simply to disappear (Figs. 1 and 2). The muscle nuclei of the affected fibers do not undergo rhexis, lysis, or pyknosis, but remain visible for some time. At most, there is some nucleoplasmic clumping (Figs. 1 and 2). The sarcolemma is preserved but it collapses and becomes increasingly difficult to distinguish from the intact stroma (Figs. 3 and 4). It looks as though the muscle fibrils had lost their syncytial integrity and had melted out or "fallen out" of their stromal envelopes. It is this appearance on a microscopic slide which suggested the colloquialism "falling-out necrosis" in use in our laboratory. No reactive exudation of polymorphonuclear leukocytes is elicited. At most, an occasional lymphocyte is present (Figs. 11 and 12). The center of the focus cleanses itself by progressive myolysis. At the periphery other muscle fibers disintegrate similarly (Figs. 11 and 12). This feature gives the process, in contrast to the *centripetal* nature of smaller and larger infarcts, a *centrifugal* character. This peripheral extension also is responsible for the fuzzy borders of focal myocytolysis (Figs. 3 and 4). Eventually, all that remains is a small focus of empty but intact cardiac stroma, in the meshes of which there are mononuclear cells, more or less laden with a finely granular, light-brown pigment (Figs. 13 and 14).

Focal myocytolysis and miliary infarcts without stromal necrosis both terminate in a fibrous tissue scar (Figs. 13 and 14). In both, this scarring is brought about largely by collapse and condensation of the preserved stroma rather than by proliferation of fibroblasts and elaboration of collagen. For neither process has the chronologic interval from onset to scarring been established. However, focal myocytolysis appears to be a more leisurely and less explosive process than infarction.

We do not know what is contained, during life, inside the loose, stromal meshwork of this focal lesion. With some exceptions about the periphery (Figs. 6 and 8), this meshwork appears largely empty. The empty appearance may be an artifact of fixation. On the other hand, the spaces may have contained a fluid so low in protein that it remained unstained. The latter hypothesis would be consistent with the

non-inflammatory character of the process. It may also, in part, account for the absence of proliferative fibrosis.

The intracellular, light-brown pigment, which has been referred to, is non-ferrous. It resembles the perinuclear pigment of muscle cells. These pigment-laden cells may be either macrophages or the nucleated, non-fibrillary remnants of partially lysed muscle fibers with their polar pigment still in place. The latter interpretation is supported by the rare observation of cross-striated fibrils within or attached to these cells. The nuclei of these cells are not distinctive enough in size, shape, or chromatin configuration to make decision of this question possible. Both interpretations as to the nature of these cells are probably valid.

In essence, then, focal myocytolysis is conceived as a local loss of myocardial syncytium, the result of a metabolic imbalance which is insufficient in intensity or duration or both to cause stromal injury or to elicit any reactive exudation. Its morphologic characteristics are: (1) disappearance of myocardial syncytium in foci usually not exceeding 1500 μ in diameter (Figs. 11 and 12); (2) absence of reactive exudation; (3) survival of the original cardiac stroma; (4) mononuclear cells containing a light-brown pigment; (5) centrifugal spread; (6) scarring of the focus by stromal collapse. There is no regenerative activity of the myocardial syncytium.*

A lesion of active focal myocytolysis (Figs. 1 to 6) as just described consists of a hypomyocytic or amyocytic center with pigment-laden cells in a loose stroma. About this there is a narrow border zone of myolysis. This centrifugal myolysis rarely occurs simultaneously about the whole circumference of all active foci. In some segments of the border of the foci one or the other of the following stages may be present:

An *inactive* or *subsiding* stage of focal myocytolysis (Figs. 7 to 10), which is characterized by pigment-laden cells lying in a collapsed loose stroma. There is no active myolysis.

A *healing* stage of focal myocytolysis (Figs. 11 to 14), which consists of more compact stromal remains and contains few or no pigment-laden cells.

A *healed* lesion of focal myocytolysis (Figs. 13 and 14), which is a tiny fibrous tissue scar, indistinguishable from a healed miliary infarct.

* In experimental narrowing of the coronary artery in young suckling pigs we have encountered a lesion similar to focal myocytolysis of human hearts. In these young animals, however, regeneration of muscle fibers did take place, as indicated by occasional muscle giant cells.

At times, one may detect the pattern of the lesion incorporated in a larger territory of myocardial infarction. This is interpreted as a sudden deterioration of a borderline metabolic imbalance, resulting not only in secondary infarction of foci already embarrassed by focal myocytolysis but also in infarction of the adjacent, previously normal myocardium.

Localization of Focal Myocytolysis of the Heart

The sequence of marginal localization and centripetal progression of reactive exudation and repair about larger cardiac infarcts has been emphasized. These large infarcts, however, display also certain centrifugal manifestations which are not usually separated from the centripetal progression. These are, first, stellate foci of myocardial disintegration which are seemingly discontinuous with the main infarct territory. Some of these are separate miliary infarcts with or without stromal necrosis but others are typical foci of myocytolysis. These lesions are situated preferentially about the external (pericardial) aspects of the infarct.

Another and uniquely centrifugal phenomenon is a discontinuous rim of myocytolysis which affects the viable myocardium of the very borders of large infarcts. This may be found long after the result of the main metabolic accident is well on its way to complete repair. It is not uncommon about the periphery of fully collagenized infarct scars. Its presence indicates that an unbalanced metabolic state may persist for a long time in such border territories.

However, myocytolysis is not confined to the borders of large infarcts. It also rims, more or less discontinuously, many miliary infarcts. Once these are transformed into scars, however, the two processes are indistinguishable.

Focal myocytolysis is also found in many hearts without infarcts, large or miliary. A favored location is the central portion of papillary muscles and trabeculae carneae of the left ventricle (Figs. 5 and 6). Fibrosis in these locations is a common finding in hearts which may or may not show diffuse fibrosis elsewhere. After these centers have become fibrotic, it is impossible to determine whether such minute loss of muscle syncytium was due to miliary infarction or to focal myocytolysis. It appears significant, however, that at the time of death centropapillary and centrotrabecular myocytolysis is much more common in these hearts than are fresh or healing miliary infarcts.

As shown by our injection studies, these centers are situated at the ends of the pure coronary vascular circulation. The metabolic exchange

of the layer of myocardium, which is situated between these centers and the endocardium proper, proceeds in part by trans-endocardial diffusion. The latter source can ordinarily nourish the subendocardial zone for a depth not exceeding the width of about a half a dozen muscle fibers. Even with large infarcts this zone frequently escapes necrosis. The width of this zone is comparable to that of the combined intima and inner third of the media of the adult aorta. This aortic zone has two similar avenues of metabolic exchange, that is, the vasa vasorum and trans-endothelial diffusion.[17]

Incidence of Focal Myocytolysis

In a detailed microscopic study of 571 hearts, an average of eleven sections were examined per heart, and each section was labelled as to its exact location; focal myocytolysis was found in 101 (17.7 per cent) hearts.* In Table I is indicated its incidence in relation to fresh

TABLE I

Incidence of Focal Myocytolysis in 571 Hearts. Association with Recent and Old Infarction

Focal myocytolysis	Recent infarcts, large and small	Fibrosis, including scarred infarcts	No infarcts, no fibrosis	Total
Present	51	45	5	101
Absent	29	233	208	470
Totals	80	278	213	571

infarcts and to fibrosis of the myocardium. The lesion was present in almost two thirds (51/80) of the hearts with recent infarcts. An almost equal number (50) of the hearts without fresh infarcts showed the lesion in question. Nearly all of these (45/50) also exhibited fibrosis of the myocardium. The 5 hearts which were free of both fibrosis and infarction were especially interesting. In them early lesions could be studied to great advantage. None of these 5 hearts had significant atherosclerosis of the coronary arteries and only one was hypertrophied. Associated clinical conditions were uremia (three) and malignant tumors (three).

Degree of Focal Myocytolysis

In the 101 hearts which displayed focal myocytolysis, a rough estimate was made of the extent of the lesion. Table II presents these

* This series of 571 hearts was studied by a method of injection and dissection previously described.[18] A correlation between the condition of the coronary arteries and the myocardial histopathology will be published subsequently.

estimates in relation to the simultaneous absence or presence of infarcts. There were 39 hearts with 1 per cent or less of myocytolysis in the total volume of myocardium examined. Such small amounts were three times as common in hearts without infarcts as in those with infarcts. There were 10 hearts with between 10 and 38 per cent of focal myocytolysis. In this group the lesion was associated with in-

TABLE II

Degree of Focal Myocytolysis in 101 Hearts

	Focal myocytolysis				Total
	Less than 1%	1.1-5.0%	5.1-10%	More than 10%	
No infarcts	29	18	1	2	50
Infarcts, large and small	10	17	16	8	51
Total	39	35	17	10	101

farcts in the great majority (8/10). The intermediate group which was losing cardiac muscle via myocytolysis at the rate of from 1.1 to 10 per cent, comprised a little more than one half (52) of the 101 hearts. In this group there were almost twice the number of hearts with infarction as without. The left ventricle was much more richly sampled in the selection of the sections than any other of the heart chambers. Focal myocytolysis is more common in the left ventricle than in the right. Hence, the degree of this lesion would be even greater had it been expressed in terms of the left ventricle alone rather than of the whole heart.

DISCUSSION

Aside from its association with coronary atherosclerosis, as has been emphasized, focal myocytolysis of the heart has been found as the predominant or incidental lesion in non-coronary diseases of man. It has been emphasized in intractable congestive failure and cardiomegaly of unknown etiology.[1,5-7] In some of these instances it has been ascribed to lues and to infections of viral or bacterial origin. It has been observed in Fiedler's myocarditis,[8] with coronary arterial embolism following subacute bacterial endocarditis,[9] scleroderma,[10] poliomyelitis,[11] uremia,[12] pregnancy and the puerperium,[5] and therapeutic insulin shock.[3]

Focal myocytolysis has been produced experimentally by oxygen deprivation in cats,[14] by adrenalin injections into rabbits,[15] by induction of hyperthyroidism, tachycardia, or both in rabbits,[16] and by diets free of vitamin B and deficient in proteins in albino rats.[13] The

lesions produced by hypopotassemia in rats[19] bear some similarity to focal myocytolysis.

The great variety of conditions in which it has been encountered suggests that the lesion constitutes the final morphologic pathway for many different etiologic agents, both natural and experimental. We conceive that the common denominator of these dissimilar agents, which produce identical morphologic changes, resides in the production of a metabolic imbalance in the heart. By this term we refer to abnormalities of tissue anabolism and catabolism such as may result from ischemia, anemia, hypotension, hypoglycemia, septicemia, toxemia, heart failure, cardiac dilatation, and nutritional disturbances.* In order to become manifest in routine microscopic sections, the metabolic imbalance will have to act with a great enough intensity and for a long enough time. The combination of these two factors may result in a degree of metabolic imbalance so slight as to cause only reversible lesions of the muscle fibers such as cloudy swelling, hydrops, or fatty infiltration. On the other hand, the degree may be so severe as to cause the irreversible necrosis of an infarct. These relationships are indicated in Table III, with the implication that the graded ana-

TABLE III

Schema of Regressive Cardiac Responses

	Degree of metabolic imbalance		
	Mild	Moderate	Severe
Lesion	Cloudy swelling Hydrops Fatty degeneration	I. Focal myocytolysis 1) active 2) inactive 3) healing II. Miliary infarct without stromal necrosis	I. Miliary infarct with stromal necrosis II. Massive infarction
Reversibility of process	Reversible	Irreversible	Irreversible
End result	Restitution to normal	Fibrous scar	Fibrous scar

tomical responses listed are not restricted to myocardial ischemia due to coronary atherosclerosis but may result also from other disturbances of metabolism. Such a concept would explain, for instance, the occurrence of any of these lesions, including infarct necrosis in the absence of significant coronary atherosclerosis. It would also explain

* Some of these disturbances of metabolism do not elicit morphologic alterations of the muscle primarily, but rather attract acute or chronic inflammatory cells resulting in some variant of myocarditis. This subject, however, is beyond the scope of this paper.

why occlusions of coronary arteries, if compensated for by a collateral circulation, need not produce a significant degree of metabolic imbalance.

The process of focal myocytolysis as it appears about the borders of an infarct was described by Smith,[4] in 1904, as follows:

"At the border of myocardial necrosis from infarction there occurs, either from the influences about to lead to solution of the dead mass, or as part of the reactive inflammatory change, sarcolysis of the ultimate fibrils of muscle through at least a short extent of the muscle fibre just outside the necrotic mass. This sarcolysis leaves, as remnants of the original fibre, structures which indicate the prior existence of a sarcolemma sheath. . . . In this solution of the muscle fibrils it is not essential that the muscle nuclei should likewise disappear, although by karyolysis they may be destroyed. . . . Such persistent nuclei are surrounded by a small amount of hyaline myoplasm and constitute the spindle-cell elements interpreted as myogenous connective tissue by some, the cells thus formed staining as does connective tissue. The fine fibrillae or membranous remnants of the sarcolemma . . . in a passive sense may contribute themselves as part of the fibrillar substance of the resultant scar. . . . The ultimate destiny of the persisting nuclei with their cell-like protoplasmic investment cannot be definitely declared. . . . The relative absence of these nuclei in the cicatrizing lesions, and the presence of small groups of pigment granules which probably mark the original situation of such nuclei, and the appearance of karyolytic changes in late stages of the process of organization in this or that example, and of atrophic forms, all speak for their eventual disappearance."

In hearts with coronary atherosclerosis the graded anatomical responses, listed in Table III, are mirrored in and overlap the clinical gradients of angina pectoris, coronary failure,[20] and myocardial infarction. The various lesser histologic manifestations—that is, the reversible degenerations, focal myocytolysis, and miliary infarcts—probably correspond to the lesser sequelae of clinical coronary heart disease. Thus, singly or in combination, they constitute the anatomical concomitants of angina pectoris and coronary failure.

Angina pectoris has long been thought to reflect cardiac ischemia or, in the broader sense here presented, metabolic imbalance in the heart. As the degree of this imbalance becomes great enough, irreversible damage to the heart muscle must follow. Various regressive cardiac responses then occur, including slowly evolving focal myocytolysis as well as more rapid miliary infarction, without or with stromal necrosis. Although such foci of irreversible muscle degeneration are not obligatory with every attack of angina pectoris, they probably develop with each episode of prolonged cardiac pain and coronary failure. Small fibrous scars in these hearts bear witness to such attacks.

Focal myocytolysis is thus compatible with all degrees of coronary heart disease, that is, with cardiac infarcts of clinical dimensions as

well as with angina pectoris and with coronary failure. On the other hand, this lesion conceivably develops without any clinical symptomatology, even angina pectoris.

This lesion may be epitomized as a focus of selective disappearance of parenchymal elements from an intact stroma, without exudative or proliferative responses. By this definition lesions identical in principle with focal myocytolysis of the heart should occur in other organs when they are subjected to disturbances of metabolism of proper degree. However, because of the inability of the heart muscle to regenerate and because of its syncytial nature, cytolysis in the heart is more readily detected. In parenchymatous organs whose constituent cells can regenerate, such as the liver, the analogous process may heal by reconstitution without leaving a trace. If the cytolysis is severe enough, reconstitution may be inadequate or incomplete, resulting in stromal collapse and fibrosis. Many a picture of diffuse fibrosis in various parenchymatous organs may have its genesis in a process akin to focal myocytolysis of the heart.

Conclusions

Focal myocytolysis of the heart is a miliary lesion which is characterized by a loss of muscular syncytium, preservation of the stroma, absence of inflammatory reaction, and eventual fibrosis.

Focal myocytolysis of the heart differs from a miliary infarct which presents coagulative necrosis of muscle, often involves the stroma, has an active inflammatory reaction, but is not different in its eventual fibrosis.

Focal myocytolysis of the heart is slower in evolution than infarction.

Focal myocytolysis of the heart is due to a lesser degree of metabolic imbalance than is miliary infarct.

Focal myocytolysis of the heart is more common than miliary infarct.

The data on incidence and degree of focal myocytolysis in the heart are based on a survey done by Dr. Priscilla Dienes Taft.

REFERENCES

1. Lisa, J. R., and McPeak, E. Acute miliary infarction of the heart. *Arch. Int. Med.*, 1940, 65, 919–932.
2. Brown, M. G.; Fienberg, R., and Holzman, D. Focal necrotizing myocarditis without interstitial infiltration. *Circulation*, 1951, 4, 909–912.
3. Akert, K. Die Insulin-Myokardose. *Schweiz. med. Wchnschr.*, 1950, 80, 1010–1015.

4. Smith, A. J. On the histological behavior of the cardiac muscle in two examples of organization of myocardial infarct. *Univ. Pennsylvania M. Bull.*, 1904–05, 17, 227–234.
5. Gouley, B. A.; McMillan, T. M., and Bellet, S. Idiopathic myocardial degeneration associated with pregnancy and especially the puerperium. *Am. J. M. Sc.*, 1937, 194, 185–199.
6. Roesler, H., and Soloff, L. A. Report of a case of left ventricular failure with unusual anatomical changes in the myocardium. *Ann. Int. Med.*, 1935–36, 9, 477–487.
7. Reisinger, J. A., and Blumenthal, B. Myocardial degeneration with hypertrophy and failure of unknown cause. *Am. Heart J.*, 1941, 22, 811–824.
8. Engelhardt, H. T., and Bruno, F. E. Fiedler's myocarditis. Report of a case. *New England J. Med.*, 1943, 228, 222–224.
9. Buchbinder, W. C., and Saphir, O. Heart failure in subacute bacterial endocarditis. *Arch. Int. Med.*, 1939, 64, 336–347.
10. Weiss, S.; Stead, E. A., Jr.; Warren, J. V., and Bailey, O. T. Scleroderma heart disease. With a consideration of certain other visceral manifestations of scleroderma. *Arch. Int. Med.*, 1943, 71, 749–776.
11. Dolgopol, V. B., and Cragan, M. D. Myocardial changes in poliomyelitis. *Arch. Path.*, 1948, 46, 202–211.
12. Durlacher, S. H., and Winternitz, M. C. Studies on the relation of the kidney to cardiovascular disease. V. Lesions of the myocardium. *Yale J. Biol. & Med.*, 1941–42, 14, 269–278.
13. Scriba, K. Über die Morphologie der Herzmuskulatur bei experimenteller Beriberi. *Verhandl. d. deutsch. path. Gesellsch.*, 1938, 31, 343–347.
14. Grundmann, E. Histologische Untersuchungen über die Wirkungen experimentellen Sauerstoffmangels auf das Katzenherz. *Beitr. z. path. Anat. u. z. allg. Path.*, 1950–51, 111, 36–76.
15. Franz, G. Eine seltene Form von toxischer Myokardschädigung. *Virchows Arch. f. path. Anat.*, 1936–37, 298, 743–752.
16. Menne, F. R.; Jones, O. N., and Jones, N. W. Changes in the myocardium of rabbits from augmenting the heart rate mechanically and from induced hyperthyroidism. *Arch. Path.*, 1934, 17, 333–355.
17. Geiringer, E. Intimal vascularisation and atherosclerosis. *J. Path. & Bact.*, 1951, 63, 201–211.
18. Schlesinger, M. J. An injection plus dissection study of coronary artery occlusions and anastomoses. *Am. Heart J.*, 1938, 15, 528–568.
19. Darrow, D. C., and Miller, H. C. The production of cardiac lesions by repeated injections of desoxycorticosterone acetate. *J. Clin. Investigation*, 1942, 21, 601–611.
20. Freedberg, A. S.; Blumgart, H. L.; Zoll, P. M., and Schlesinger, M. J. Coronary failure. The clinical syndrome of cardiac pain intermediate between angina pectoris and acute myocardial infarction. *J. A. M. A.*, 1948, 138, 107–114.

[*Illustrations follow*]

LEGENDS FOR FIGURES

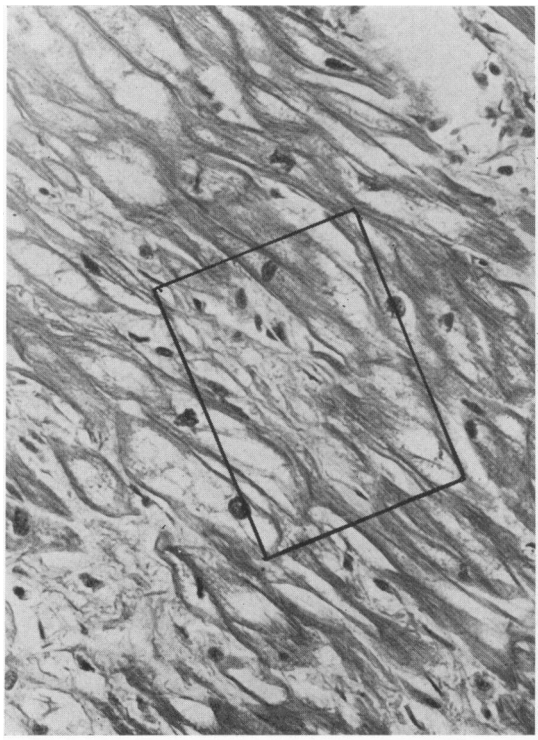
All sections were stained with hematoxylin and eosin.

FIG. 1. Earliest active stage of focal myocytolysis. Borders ill defined. Hydropic degeneration of muscle. Longitudinal section. × 185.

FIG. 2. High-power view of Figure 1. Active myocytolysis. Residual muscle nuclei intact. Muscle fibers frayed and blend imperceptibly with the rarefied cardiac stroma. Some nondescript remnants of the lysed muscle still contained within the sarcolemma. No stromal reaction or cellular exudate. × 475.

FIG. 3. Early active stage of focal myocytolysis. Three foci. Each focus abuts with at least one border upon a small interfascicular septum, accounting for the sharp borders over some part of their circumference. Borders are fuzzy where in contact with cardiac muscle. Cross section. × 185.

FIG. 4. High-power view of Figure 3. Disintegration of muscle fibers by fragmentation and myocytolysis. Seeming increase of nuclei is due to approximation of stromal and muscular elements rather than to proliferation or regeneration. Remaining muscle fibers small and of irregular shape, but nuclei are intact. No cellular exudation. × 420.



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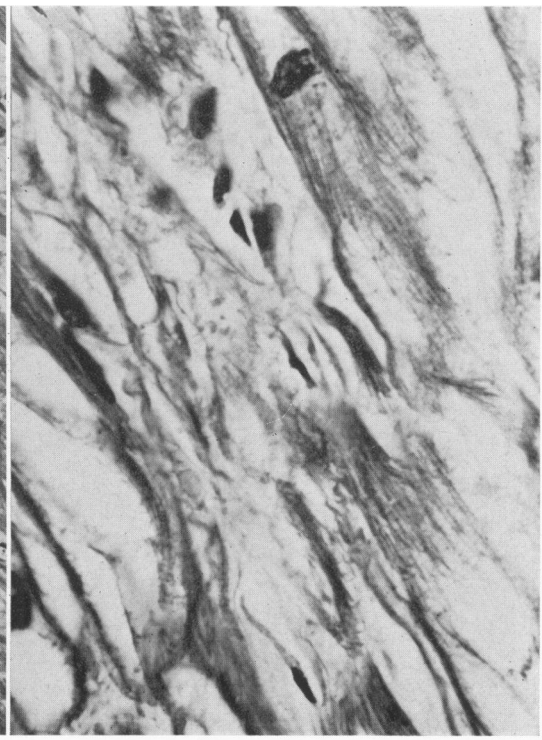

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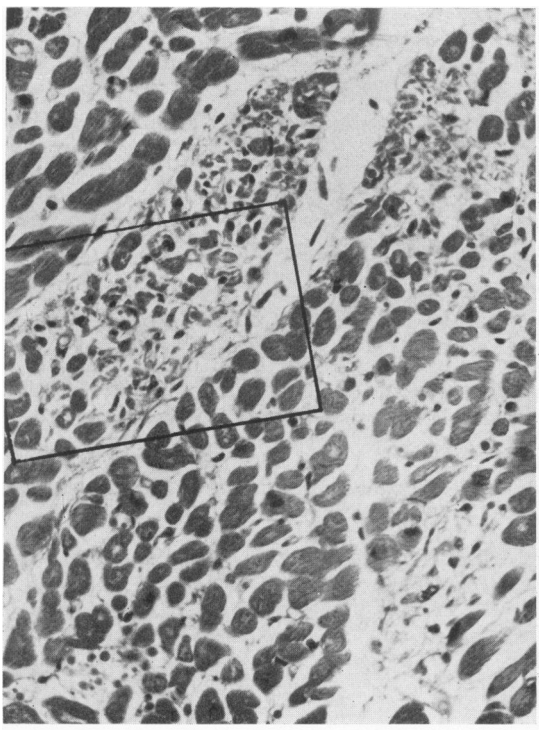

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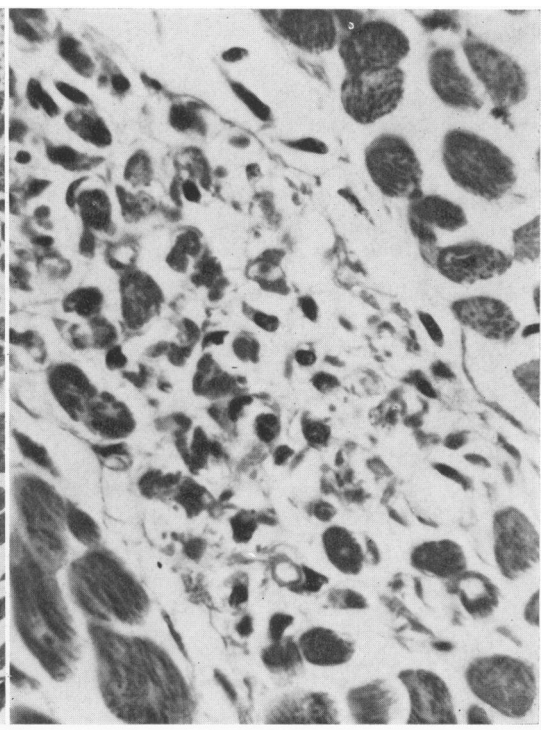

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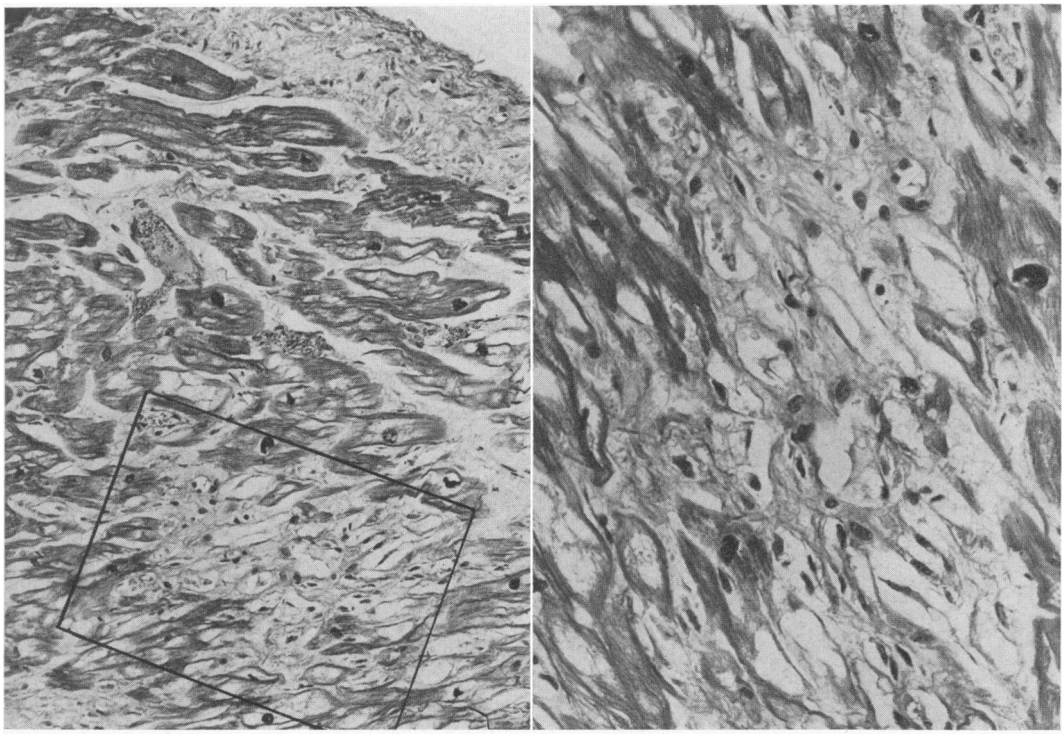


Fig. 5. Active stage of focal myocytolysis. Subendocardial focus in a papillary muscle. Centrifugal myocytolysis indicated by fuzzy borders. Longitudinal section. × 92.

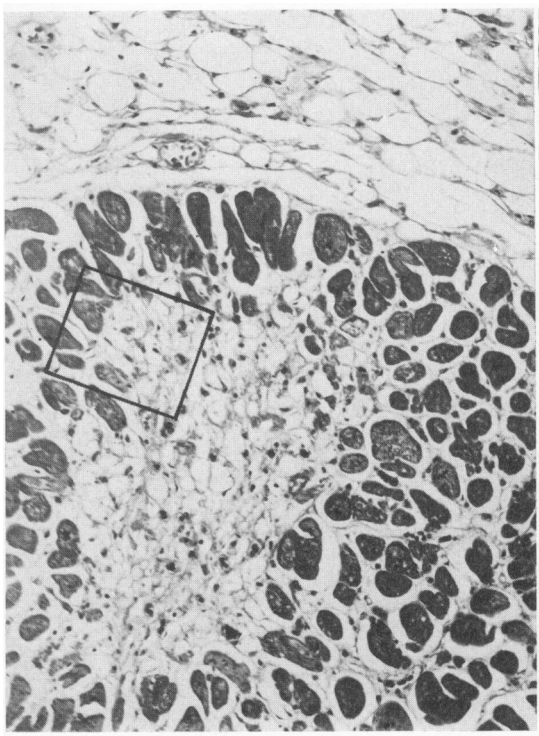
Fig. 6. High-power view of Figure 5. Active myocytolysis with fraying and splitting of involved muscle fibers. Rarefied sarcolemmal sheaths generally empty but a few contain either sparse myofibrils or a scalloped thin protein matter. No cellular exudation. × 185.

Fig. 7. Subsiding stage of focal myocytolysis. Subepicardial focus. Borders both sharply delineated and fuzzy. There is a certain resemblance between the empty stroma of focal myocytolysis and of the epicardial fat tissue. Cross section. × 92.

Fig. 8. High-power view of Figure 7. Detail from the sharp border. Isolated bits of unaltered muscle fibers inside sarcolemmal sheaths. Majority of sarcolemmal sheaths empty; a few contain foamy protein precipitate. Stroma intact. × 475.

Fig. 9. Subsiding stage of focal myocytolysis. Borders fairly quiescent. Empty cardiac stroma slightly collapsed. Cross section. × 92.

Fig. 10. High-power view of Figure 9. A few isolated fiber fragments exhibit disorderliness of myofibrils. No active myocytolysis. Stromal details well defined. Capillaries generally empty. × 185.



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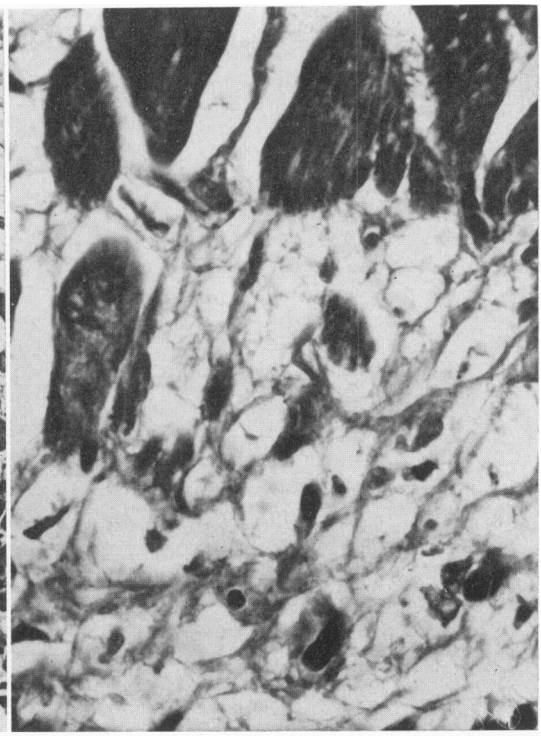

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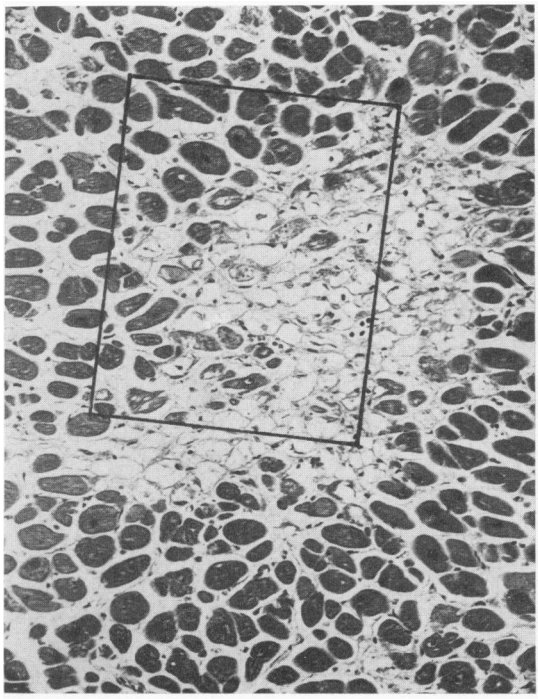

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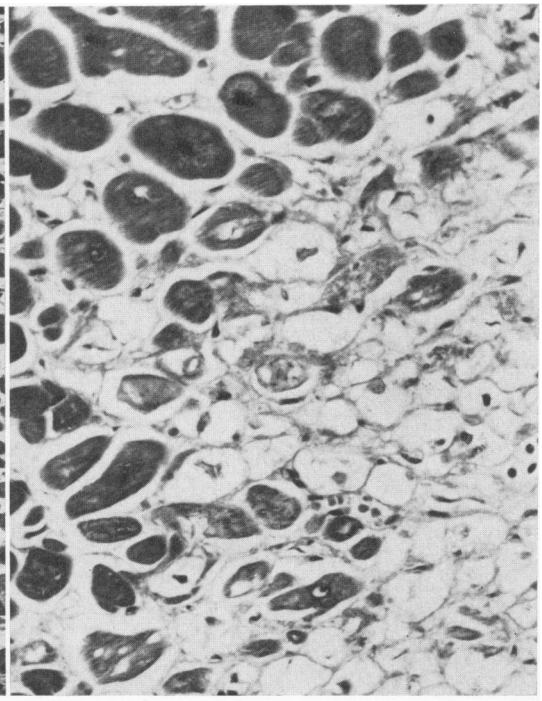

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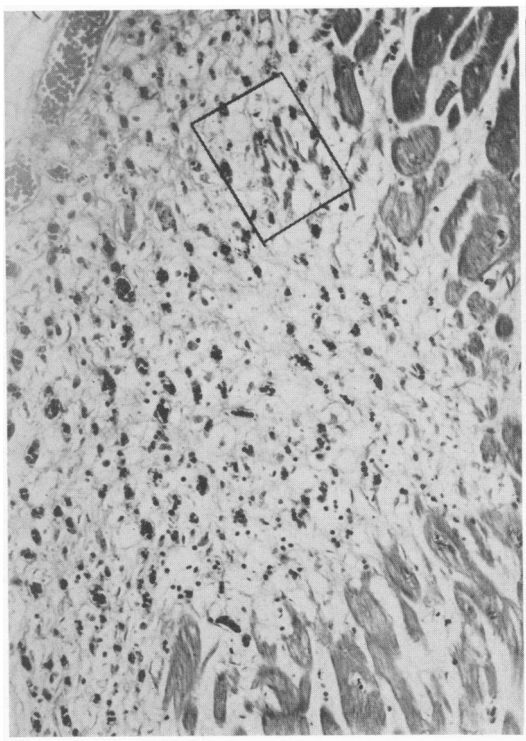
FIG. 11. Healing stage of focal myocytolysis. Edge of a larger focus (1500 by 700 μ). Some residual myocytolysis with a scattering of lymphocytes. Stromal reticulum empty and approximated. Capillaries engorged. × 94.

FIG. 12. High-power view of Figure 11. Attenuated remnants of cross-striated muscle. Other sarcolemmal sheaths either empty or containing a fine network of eosinophilic material. Congestion of capillaries. × 485.

FIG. 13. Healing and healed stage of focal myocytolysis. Two subepicardial foci. The upper focus is healing. Borders sharp. Periphery still composed of loose cardiac stroma. Central stroma collapsed. The lower focus is almost healed (fibrous scar). Borders quiescent. A few entrapped atrophic fibers toward 3 o'clock. Cross section. × 100.

FIG. 14. High-power view of Figure 13. Healing focus. A few small but viable muscle fibers entrapped. Collapsed stroma in center. No myocytolysis. No stromal cell proliferation. No inflammatory cells. × 200.



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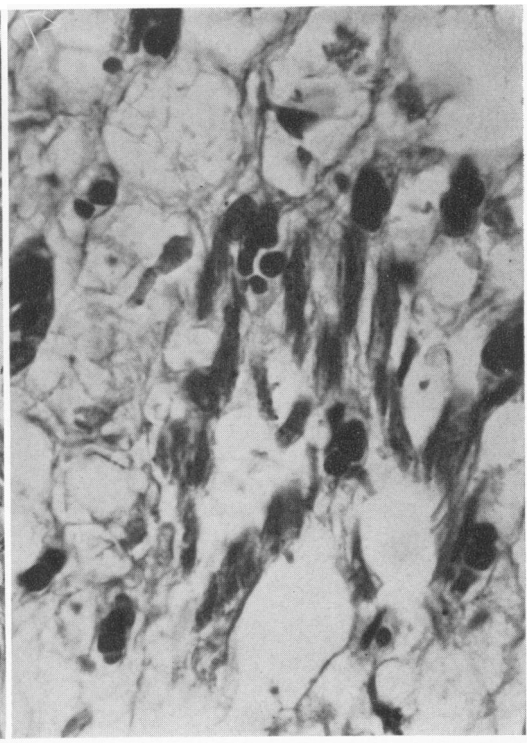

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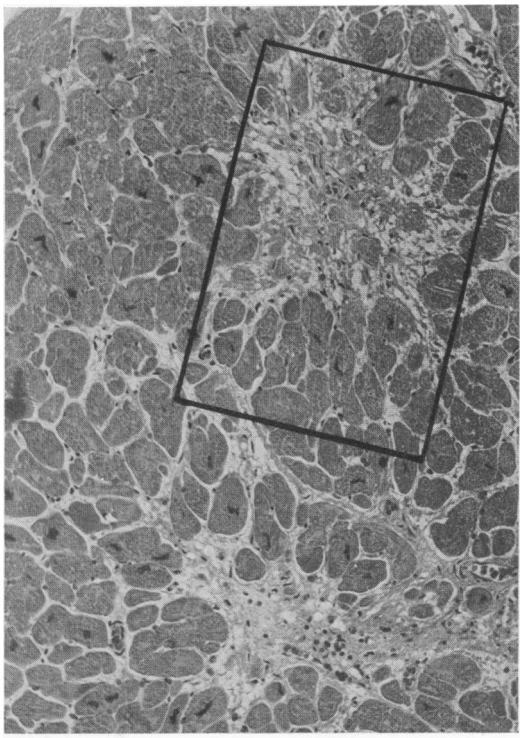

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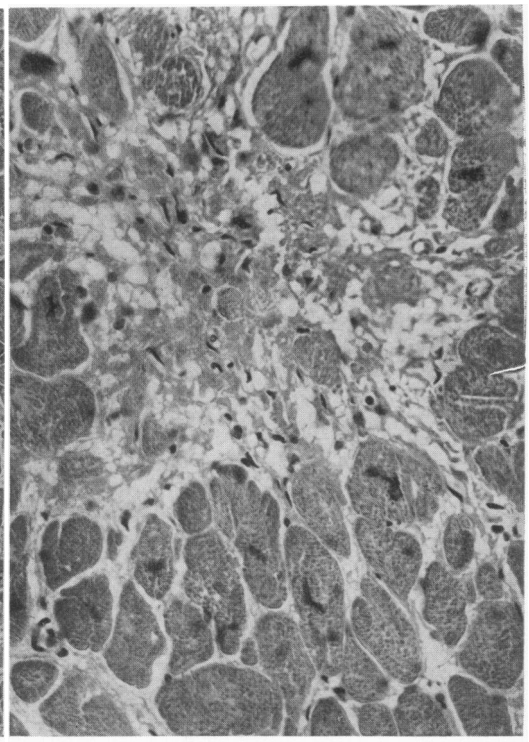

14