AN ANATOMICAL AND EXPERIMENTAL STUDY OF SEGMENTATION OF THE MYOCARDIUM AND ITS RELATION TO THE INTERCALATED DISCS*

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This study was undertaken in order to learn the nature of segmentation and fragmentation of the myocardium. Segmentation is ordinarily considered to be separation of the muscle fibres within the intercalated discs and fragmentation usually signifies separation at points in the fibres between the intercalated discs. These definitions are not uniformly accepted but represent the views of most investigators. This study considers the point of separation, the associated conditions in the heart and body generally, the relation to the intercalated discs and the genesis of the lesion. The human material represents a wide variety of acute and chronic diseases. Although more than 500 hearts have been examined, the more exact study has been confined to 100 hearts, which exhibited separation of the fibres and were classified as the seat of segmentation or fragmentation according to the definitions given above.

Leuwenhoeck [1] made the first attempt to determine the structure of myocardial tissue. In the study of hearts of oxen, sheep and ducks he found the muscle elements to be connected to form a net-like structure. Passing over the works of the next century and a half we come to the group of investigators who worked with modern section technique. Quotation from all of these earlier workers would lend unnecessary bulk to the discussion and hence only the more important will be mentioned. Eberth [2] described transverse lines in the muscle elements of the heart, to which he gives the name "Verdichtungsstreifen." Schweiger-Seidel [3] described the same. Referring to them, this author says that refractile lines are present in certain areas dividing the muscle elements into cells. Wagener

* Received for publication June 16, 1924.

was the first to introduce the idea that the myocardium is not composed of independent cells. Ebner [4] expresses this idea very clearly. The so-called cement-lines or cell borders do not have the significance formerly ascribed to them, since well defined cell borders of this order do not exist. He believed that the cell boundaries of previous authors were either due to contraction of muscle at the time of death or were margins of torn parts of the perimysium. He, as well as Wagener,[5] therefore, considered the myocardium as a syncytium, rather than independent cells connected by cement substance. Schaffer [6] likewise supports the idea that the cement lines are due to local contraction at the time of death and refers to them as "Verdichtungsstreifen." MacCallum [7] and Hektoen [8] described the same as "cement lines." Heidenhain,[9] in a work which is very important for our investigation considered the transverse lines as intercalated discs or "Schaltstücke" and considered them points of muscle growth. Of this work we shall speak more later. Palcsewska [10] and Werner [11] working with Zimmermann [12] combated the work of Heidenhain and attempted to support the cellular rather than the syncytial view concerning the structure of heart muscle. Marceau [13] believed the intercalated discs to be small tendons, interspersed in certain places throughout the cardiac muscle. Diettrich [14] considered them as points of increased strength in the muscle elements. Tawara [15] and Mönckeberg [16] found cement lines in the atrioventricular bundle of Hiss; but Aschoff [17] considers such lines as different from those of ordinary heart muscle. Ogata [18] considers the cement lines as mere mechanical aids. Jordan and Steele [19] refer to the cement lines or transverse lines as "intercalated discs" and say "the presence of discs would seem to be correlated with the function of rhythmic contraction of cardiac muscle and may represent a fixed phase of contraction wave (local or general) or more probably is the result (of the nature of an irreversible strain condition) of the total amount of function." In connection with this we may mention the fact that Diettrich [20] has shown that ligation of the ascending aorta in rabbits in which he obtained a slight hypertrophy will lead to more pronounced intercalated discs.

It seems unnecessary to give in detail the development of the history of fragmentation and segmentation since it is to be found with complete references in Hektoen's[21] article. We shall only allude to Virchow[22] as having described the condition in the year 1847, but since, at this time exact knowledge of the structure of cardiac muscle was lacking, his own work was, of necessity, imperfect. In most modern textbooks of pathology and in the view of most pathologists the lesions of segmentation and fragmentation are distinct. In Delafield and Prudden's[23] textbook for instance, is found the statement that "examination shows loosening of the muscle cells from one another as if by some change in the cement substance, — 'segmentation' — or the fibres may be broken across — 'fragmentation.'"

Among French authors considerable work has been devoted to the subject, especially by Renaut,[24] who believed fragmentation to be a distinct disease, — "Myocardite essentielle, chronique segmentaire." Von Recklinghausen[25] originated the opinion that fragmentation arose during the death agony, due to the final convulsive contraction of the heart. Streckeisen[26] particularly supports this view since in hearts, the seat of fragmentation, he was unable to find degenerative changes in the parenchyma or reactions in the interstitial tissue. Karcher[27] considered it a retrogressive change and believed that it could lead to sudden death during the course of chronic diseases. Hektoen,[28] who believes in heart muscle cells, says that cells are loosened in fragmentation but "the fate of loosened muscle cells is not known." Browicz[29] considers that extensive fragmentation may cause functional derangement of cardiac muscle with failure or even sudden death. However, he does not recognize primary fragmentation as a distinct disease. MacCallum[30] and Hektoen[31] support the view that fragmentation may cause mitral insufficiency.

Another important idea has been advanced to explain this condition, i. e., that fragmentation is due either to artefacts of technic or to post-mortem change. Buhlig[32] believes that local fragmentation may be produced by the microtome, while Tedeschi[33] and Israel[34] consider the artefact origin as impos-

sible. Dunin [35] states that putrefaction may produce a picture similar to fragmentation, but Kaufmann [36] terms this type of dissolution "Dissoziation."

Regarding the direct relation between intercalated discs and fragmentation we again have a diversity of opinion. Israel [37] and Oesterreich [38] do not believe that cement lines are the seat of the lesion, as is also the opinion of Schlater [39] from a study of two cases. However, Schlater, as well as Marceau,[40] considers cement lines to be intramuscular tendons. Schlater remarks that in cases in which fragmentation is present in the cement lines the myocardium must be in some way abnormal or be the seat of injury. Stamer,[41] as a result of his work concedes that there are fractures through cement lines (segmentation) as well as through muscle body (fragmentation). Both types may occur simultaneously. Probably both have the same cause, i. e., convulsive contractions occurring at the moment of death. Segmentation alone cannot have this explanation. It is not certain whether putrefaction may cause a decomposition of the heart muscle which is represented as separations of the fibres. Another somewhat related theory as to etiology is that of Giese,[42] who considered it probable that intestinal bacteria reach the heart during the agonal period and they, through the production of gas, produce fragmentation and segmentation.

Concerning experimental production of fragmentation, Karcher [43] believed that it could be produced in rabbits' hearts but identified the lesion only in teased preparation. Stamer [44] repeated the experiments with negative results and criticizes the technique as faulty. Lissauer [45] attempted to produce fragmentation and segmentation in rabbits by chloroform narcosis, lead poisoning, air emboli and also by ligation of the abdominal aorta. He succeeded in some instances but stated that because of numerous failures the experiments were unsatisfactory. Aschoff [46] considers that experimental work on post-mortem specimens has never successfully produced fragmentation or segmentation.

This survey is offered to show the divergence of opinions concerning the nature of intercalated discs, segmentation and

fragmentation, and briefly to summarize the present status of the subject.

Studying first in our material the so-called fragmentation, microscopical examination reveals that fragmentation seems to occur in the muscle body. The field shows numerous broken muscle fibres, their margins being irregular, depending on the injuring force, and the resistance of the fibres. As pointed out by Hektoen we also find small muscle fragments, often without nucleus, sometimes to a marked extent the predominating form of disunion. In some cases we find fragmentation in nearly every field, in others only in places; we are also able to distinguish (MacCallum) breaks in the contracted and in the extended muscles. Careful examination of the fractures shows that they are irregular in character but the irregularity is varying; this variation being zigzag, combform, step-like and also in some cases wavy. There is no regularity in the breaking places of the fibres. In studying the ends of the ruptured fibres by the use of various stains and by the examination of numerous fields of vision we observe on the places of rupture fine lines. They are particularly well brought out by the use of Heidenhain's technique with either brilliant black or B-naphthol-black. (These were Pond's Dye Stuffs and were equally satisfactory.) These lines seem to follow the border of the broken fibres with their various contours. At times a line at each end of the ruptured fibre is seen clearly and again only at one end, while the opposite end does not show the line. We also have seen ruptured fibres with no line at all. The reason for not finding these lines may be due to their absence in our particular plane of vision. Inasmuch as the section is not cut entirely parallel to the course of the fibres, the opposing ends of the ruptured spot must be in a higher or a lower place.

Insufficient study of the rupture places will make it appear that muscles are broken irregularly. Our observations, however, indicate that irregularities exist, these being demonstrated in the delicate lines described before. According to their shape and staining affinities they are considered to be intercalated discs. Normal muscle fibres in these cases show many distinct intercalated discs, clearly demonstrable by the

hematoxylin-eosin stain. The intercalated discs vary in shape, the majority being irregular and zigzag, only a few step-like and none straight. It is unnecessary to add anything further on the subject of fragmentation as it would be only a repetition of observations described by others.

In our material the pictures of segmentation show a regular appearance; the fibres are segmented. The lines of segmentation are distinct intercalated discs. A few appear step-like or crooked. This has also been reported by Hektoen. The intercalated discs are especially distinct by the use of brilliant black, B-naphthol-black, Bender-Heidenhain, etc. Often we discover intercalated discs on both ends of the separated fibres; sometimes only one can be recognized. The reason probably is that there may be a dislocation in a cross direction, or the section is not exactly parallel with the course of the fibres. We find general or localized segmentation, sometimes in a portion alone. Some segments are larger, others smaller; some with, some without nucleus, but in the last type of fracture the borders have a straight course also. Here too, we are able to find as noticed already by Stamer, in the intact muscle fibres, clear and distinct intercalated discs. The discs in these cases are more numerous and clearer than in hearts without segmentation. But the majority are straight, and only a few step-like. They are visible when hematoxylin-eosin stain is used.

As a result of the observations just recorded it would appear that the differences between fragmentation and segmentation are apparent rather than real. Segmentation shows a sharp straight border at right angles to the long axis of the fibre; the intercalated disc is clearly visible at the edges of the fracture. Although in fragmentation the lines of fracture show much irregularity, nevertheless we find almost uniformly some definite indication of the presence of intercalated discs, which, as will be shown subsequently, are irregular before fracture.

It may seem paradoxical to combine the conception of segmentation and fragmentation by bringing the intercalated discs in connection with fragmentation, but other investigators also have found a relation between these states. Browicz,[47] for instance, states that the conspicuous appearance of the discs is

the initial phase of fragmentation. Jordan and Bardin,[48] and Jordan [49] discussed the relation between intercalated discs and so-called segmentation and so-called fragmentation. They come to the following conclusions: "Rupture of cardiac muscle fibres always occurs in relation to the intercalated discs. Segmentation and fragmentation are therefore not to be distinguished on the anatomical basis of rupture; segmentation and fragmentation are probably the same process, exhibited in different degrees of severity."

This leaves open the question as to why, when the underlying process in the two changes is the same, the histological picture should be superficially different.

When the intercalated discs are the places of rupture, it must be realized that they are predisposed places, otherwise the fracture would not occur just in the intercalated discs. If they are predisposed to fracture it would be hard to believe that they were contracted muscle fibres or a fixed phase of the contraction wave, as some authors have believed. There is no reason for believing that contracted muscle fibres would tear so easily. We therefore assume that the intercalated disc must be a *punctum minoris resistentiae* in a fibre from a dilated heart. Why dilatation must precede will be explained later. On the basis of our own work and that of others we shall attempt to explain why segmentation and fragmentation always occur in the discs, the variations in their shape, the regularity and irregularity of segmentation and fragmentation, both inseparably linked to the intercalated discs. Heidenhain's old theory will serve to explain the intercalated discs as a *punctum minoris resistentiae.*

Heidenhain does not believe in the existence of heart muscle cells. After a considerable study he offers the hypothesis that the intercalated discs, as he named the cement lines, are growing parts that provide longitudinal growth and deliver material for the building up of new muscle at both ends of the segmenta. The intercalated disc is the matrix substance of the daughter fibres. Only at this place will there be formation of new muscle fibres. He shows further that the basal membrane of Krause — appearing higher or lower than the discs, from

TABLE 1

Age	General Disease	Heart Disease	Heart Weight grams	Time between death and autopsy	Results
8	Acute purulent pleurisy	...	210	15 hrs.	S
16	Typhoid fever	...	220	...	F
18	Pneumonia	D	225	...	F
20	Accident	...	350	...	S
20	Tumor of the brain	...	400	48	F
23	Acute suppurative cholecystitis	D	250	18	F
24	Carcinoma recti	Cl. sw.	175	...	S
24	Pneumonia	...	375	...	S
24	Acute cholecystitis	Cl. sw.	325	7	S
25	Dif. peritonitis	D	300	...	F
25	Accident	...	300	...	F
25	Necrosis of liver	...	...	1	F
26	Nephritis, chr. par.	D	350	2	S
26	Peritonitis — acute	...	250	16	F
27	Diph. laryngitis	...	210	15	S
28	Tuberculoma of the brain	Cl. sw. H	300	...	F
29	Dif. nephritis	Cl. sw.	355	21	F
30	Pneumonia	Cl. sw.	370	...	F
30	Cerebral hemorrhage	Ac. endocard, H.D.	410	5	F
30	Pneumonia	D	300	5	F
31	Subacute endocarditis	D. H.	380	...	F
32	Nephritis, chr. interstitial	D	300	4	S
33	Meningo-encephalitis, tbc.		280	6	S
33	Pneumonia	Cl. sw.	450	...	F
33	Pulmonary edema	H. D. F. ch.	350	...	F
34	Syph. mesaortitis, pneumonia	D. H.	290	9 days	F
34	Pernicious anemia	H. fat. degen.	500	46	F
35	Cirrhosis of liver	...	325	20	S
35	Carcinoma of cervix uteri	Fat. degen.	300	...	F
35	Pneumonia, sec. contr. kidney	D. H.	550	6	F
36	Acute peritonitis	...	375	18	F
37	Chronic valvulitis	H. D. Cl. sw.	675	...	F
38	Carcinoma of liver	...	375	7	S
38	Glomerulonephritis	H. D.	650	20	F
38	Mural endocarditis multiple thrombi in the pulmonary arteries. Infarction and abscess of the lungs	...	265	15	F
40	Diffuse nephritis	H Chr. Myo.	335	...	F
40	Tbc. pleurisy, subacute pericarditis	...	...	...	F
40	Myomalacia cordis	H. D.	440	18	F
40	Congest. of the lungs	...	200	6	S
40	Chronic par. nephritis	...	300	6	S
40	Purulent peritonitis	D. cl. sw.	300	7	F
40	Pneumonia	D. H.	675	...	F
42	Chr. dif. myocarditis	H. D.	765	47	F
42	Septicemia	...	350	6	F
45	Luetic mesaortitis	H. D.	485	...	F
45	Ulcerative enteritis — acute	D	400	30	F
45	Pneumonia	...	325	10	F
45	Pachymeningitis	...	265	5	S
45	Glioma cerebri	...	320	...	F
45	Chr. endocarditis and myocarditis	D. H.	550	5	F
45	Edema of the lungs	D. H.	775	...	F

Age	General Disease	Heart Disease	Heart Weight grams	Time between death and autopsy	Results
46	Dif. cellulitis	Fat. degen.	475	6	F
47	Acute valvulitis, chronic valvulitis	H	575	...	F
47	Acute vegetative valvulitis	H	640	...	F
47	Pneumonia	...	300	20	F
49	Leptomeningitis	...	350	9	F
50	Pneumonia	...	440	36	F
50	Pneumonia	...	340	2	F
50	Acute ulcerative ileocolitis	...	375	...	S
50	Melanotic sarcoma of the eye	...	...	...	S
51	Dif. cellulitis	H. D.	410	36	F
51	General arteriosclerosis	H. D.	555	4	F
54	Multiple emboli portal vein	H. D.	...	...	F
55	Sinus thrombosis	...	260	4	S
55	Acute pancreatitis	Cl. sw.	350	...	F
55	Chr. interst. nephritis	D. H.	500	8	F
56	Pneumonia	D	350	11	F
57	Pneumonia	D	350	9	S
60	Chronic nephritis	H	550	16	F
60	Luetic mesaortitis	H. D.	1095	6	F
60	Hemorrhag. cerebri	...	325	72	S
60	Pneumonia, endocarditis	H	535	1½	F
62	Pleurisy — tbc.	Tbc. pericar.	350	72	F
65	Peritonitis	Cl. sw.	315	...	S
65	Generalized suppurative peritonitis	Cl. sw.	295	...	F
65	Thrombosis of small branch of super. mesenteric artery	H	600	...	F
67	Chronic gastric ulcer	D	335	...	F
68	Prostat. hyper.	D	315	...	S
68	Obliterating arterioscler. of coronaves.	Myocard.	325	7	F
68	Nephritis, degen. and product.	H. D.	650	8	F
68	Carcinoma of stomach	Cl. sw.	235	5	F
70	Sclerosis of coronary artery	D	350	8	F
70	Emphysema	H. D.	475	24	F
70	Pneumonia	...	290	24	S
75	Thrombosis of the mesenteric artery	...	300	6	S
AGES NOT KNOWN	Peritonitis	D	295	...	S
	Miliary tbc. of lungs	Cl. sw.	375	...	S
	Pneumonia	...	275	...	S
	Myocarditis	Fat. degen. D. H.	410	3	F
	Accident	...	315	...	S
	Acute passive congestion of lungs	D	300	...	F
	Meningitis	...	290	10	F
	Chr. diffuse nephritis	H. cl. sw.	500	...	F
	Tbc. pneumonia	...	225	4	F
	Chronic nephritis	...	315	5	F
	Pneumonia	...	275	4	F
	Chronic leptomeningitis	...	...	14	S
	Carcinoma of esophagus	H. cl. sw.	290	2	F
	Pulmonary gangrene	D	275	...	F
	Pontine hemorrhage	Cl. sw.	225	...	F

* Abbreviations:

H — Hypertrophy.
D — Dilation.
Cl. sw. — cloudy swelling.
Fat. degen. — Fatty degeneration.
F. ch. — Fatty change.
Ac. endocard. — Acute endocarditis.
Chr. myo. — Chronic myocarditis.
Tbc. pericard. — tuberculous pericarditis.
F. — Fragmentation.
S. — Segmentation.

one end of the longitudinal direction of a fibre to the other ("concordans") — goes up in the region of the disc to the disc, and does not cross the entire latitude of the first at this place. To the question as to why we are able to see the development of the heart tissue in a full grown heart, he replies that the development as elsewhere does not stop all at once, but is literally "a falling asleep step by step" so that we are able to see each phase of the development.

Against this theory considerable opposition has arisen. The majority of authors oppose the theory on the basis of the fact that we never find intercalated discs in the fetal period and in early childhood in which, if present, the discs should be prominent if they are indeed growing parts. It can, however, be supposed that at these early periods the discs, being growing parts of the muscle tissue, although physiologically different may not be histologically distinguishable. Later, after suspension of their function has occurred, they change and become visible by our method of staining.

The intercalated discs are, after suspension of their function, weaker than the other parts of the muscle fibres which have no function with regard to growth. Not considering the peculiar condition of the "basal membrane," their loss of function is the cause of their fragility and the reason why we may call them a *punctum minoris resistentiae.*

As we have shown before, the places of rupture of the muscle fibres are the same in segmentation as well as in fragmentation — the intercalated discs. To explain why the same place of rupture produces different pictures, in one instance practically straight rupture lines, and in the other quite irregular ends, the following is offered.

Table I gives the data of 100 hearts showing segmentation or fragmentation. The hearts originated mostly from autopsies performed in the Pathological Department of Lakeside Hospital. We fixed the tissue in formalin or Zenker's fluid and stained by various methods as hematoxylin-eosin, Heidenhain's [50] blue-black and B-naphthol-black. A few hearts have been obtained from autopsies performed in the City Hospital and Mt. Sinai Hospital in Cleveland.

We see accordingly that fragmentation and segmentation may happen in every disease nearly, as may be clearly seen in Table II. We found fragmentation and segmentation in patients dead with diseases predominant in the following organs.

TABLE II

Heart	10
Vessels	10
Larynx	1
Lung	7
(Pneumonia)	18
Pleura	3
Esophagus	1
Intestines	5
Peritoneum	7
Liver	6
Kidney	11
Prostate	1
Uterus	1
Brain	11
Accident cases	3
General diseases	5

Pneumonia is the most frequent cause of death in this series. Concerning the age of the patients we may say that fragmentation and segmentation may occur at any age between 20 and 70 years. Only in two cases did we find fragmentation in younger individuals. We also see in the tables that the time between death and autopsy does not play a rôle in the appearance of segmentation and fragmentation. The difference in time is from one hour to 9 days.

In 41 per cent of the autopsies performed we found fragmentation and segmentation. A comparison between fragmentation and segmentation on one hand and hypertrophy of the heart on the other hand leads to the following: In 73 cases showing fragmentation 31 took place in hypertrophic hearts; in 27 cases showing segmentation, no heart shows hypertrophy.

It is probable that the difference between hypertrophic and non-hypertrophic hearts, as regards fragmentation and segmentation, lies in the variations in the intercalated discs.

Jordan [51] shows that the hypertrophic heart is characterized

by a "specific type of discs." He names this type "comb type" and believes that the normal disc is "changed by process of the action of simple mechanical factors of transverse and longitudinal tension, such as obviously prevail in hypertrophic fibres." In one of his pictures we can demonstrate the characteristic comb form of intercalated discs. Fracture or separation along such irregular lines would produce the appearance ordinarily called fragmentation. In normal hearts such irregular discs are unusual and the picture of segmentation is more characteristic. Fragmentation, however, is not constant in hypertrophic hearts and may occur in normal hearts. Our further studies show that this is not due to differences in the processes of fragmentation and segmentation but due entirely to situation and conformation of intercalated discs.

We must assume that fragmentation and segmentation are dependent upon two factors, one being the intercalated discs and the other the pressure changes in the ventricles. Considering the first factor we may say that the intercalated discs are *ready for separation* when they are weaker than normal. The other factor, which must produce traction upon the fibres and discs, is acute dilatation of the chambers, a condition which commonly occurs immediately before death. In order for fracture to occur both factors must play a part, for if the intercalated discs were strong enough no separation would occur and if there were no traction there is no reason for a break of continuity. If "readiness for separation" were not essential, all dilated hearts would show the break of fibres, but we have as yet no facts to point to the origin of this local weakness.

Observation demonstrates changes in the intercalated discs before rupture, principally in the nature of stretching or enlargement so that they become unduly prominent. This explains the change observed by Browicz [52] as the first step of fragmentation. In the non-hypertrophic heart this is followed immediately by fracture in more or less straight transverse lines giving the picture of segmentation. In the hypertrophic heart with dilation or in other hearts the seat of marked dilatation, the enlarged discs show step-like and comb forms. When fracture occurs it is in the irregular lines of what has been

called fragmentation. Such fracture, however, follows the lines of previously distorted discs and is in reality only another manifestation of segmentation. But it is possible that the intercalated discs may break in either or both of these phases, if a sudden increase of the dilation occur. Thus, we may find fragmentation in a non-hypertrophic heart, and intercalated discs with comb forms without a separation of the fibres.

Experimental Data. Assuming that there are two factors, weakening of the intercalated discs and traction by dilatation, experiments were performed as follows. An attempt to produce dilatation without opening the thorax was made in four rabbits. The abdominal aorta was ligated just below the celiac axis and both carotid arteries were ligated in the neck. The gastro-colic and hepatic branches of the celiac axis were ligated. Fifty cubic centimeters of 0.85 per cent salt solution were injected into the splenic artery. No dilatation of the heart resulted and there was no segmentation. With the assistance of our colleague, Dr. M. L. Richardson, the ascending aorta was ligated under artificial respiration. The ligature was complete for a total of five minutes with an interval of free circulation for one minute after each minute of closure. Marked dilatation of the left ventricle was produced. Microscopic examination showed in all instances marked segmentation in straight transverse lines. Even with the hematoxylin-eosin stain it was plainly seen that this line of fracture was through the intercalated discs. The intercalated discs elsewhere were prominent, in striking contrast to the non-dilated hearts, in which it was difficult to find intercalated discs. Six other rabbits, anaesthetized under the same conditions for a similar period, but without ligation, failed to show prominence or separation of the intercalated discs. In two rabbits, ligation of the pulmonary artery was followed by changes in the right ventricle identical with those produced in the left ventricle by ligation of the aorta. Ligation of the aorta of three dogs and two cats was followed by histological changes similar to, but not so marked as, those in the rabbits.

Phosphorus and epinephrin were employed in an attempt

to produce conditions in the myocardium comparable to those hypothetical alterations which presumably produce weakening of the intercalated discs in man. Ten rabbits were given each 4.0 mgm. phosphorus per kilogram in olive oil by stomach tube, daily for eight days. Three were used as controls and in five the ascending aorta was ligated under artificial respiration as in the preceding experiments. The dilatation of these hearts was not nearly so marked as in the other animals not treated with phosphorus and histologic examination showed less marked segmentation and no prominence of intercalated discs. The controls showed neither segmentation nor prominence of intercalated discs. All show fatty degeneration.

Epinephrin was administered intravenously to eight rabbits in daily doses of 0.5 c.c. of a 1: 5000 dilution for fourteen days. This was found to be the largest dose that could be tolerated for this period. Two weeks after the last dose of epinephrin five were subjected to ligation of the ascending aorta as in the previous experiments and three were used as controls. In these animals dilatation was not so marked as in other animals not treated with epinephrin, and disappeared with greater rapidity in the intervals. Histologically, the intercalated discs were not prominent and there was only moderate segmentation, always in straight lines and in the intercalated discs.

In order to determine whether or not segmentation is compatible with life two otherwise normal rabbits were subjected to ligation of the ascending aorta as described above under aseptic conditions and the thorax closed. Both recovered quickly from the ether anaesthesia and appeared to be in excellent condition, eating well and maintaining the usual bodily activity. One was killed 24 hours and the other 48 hours after operation. The hearts were not dilated at necropsy. Histologically, moderate segmentation was found, in straight transverse lines in the intercalated discs. In other parts the intercalated discs were not prominent.

These experimental studies tend to confirm the view that there is only one type of fibre fracture, namely, that which occurs in the intercalated disc. Such segmentation can be produced by marked dilatation of the heart whether otherwise

normal or the seat of fatty degeneration in phosphorus poisoning. In fatty degeneration as produced here and following the prolonged administration of epinephrin, the dilatation following ligation of the aorta is not so marked as in the normal heart and correspondingly the segmentation is less evident. Similarly, the intercalated discs are not so prominent as in the normal hearts. This suggests that if the strength of intercalated discs be constant the degree of segmentation is roughly proportional to the degree of dilatation. From the study of the human material segmentation is confined almost entirely to dilated hearts. Aschoff in a personal communication states that upon examination of soldiers killed in action he was unable to demonstrate segmentation until after rigor mortis had set in. We are not too ready to apply the results in the rabbit heart to human material but the results are strikingly suggestive. Some of the rabbit hearts showed ventricular fibrillation and others did not. Hence, it cannot be assumed that such fibrillation is of significance in this connection. In a personal communication Biedl supports this view. Finally, it can be said, at least in reference to the rabbit heart, that segmentation is not necessarily an agonal phenomenon since two rabbits survived in apparently perfect condition.

Conclusions

1. The intercalated discs appear to be points of least resistance when the heart is subjected to distention.

2. Separation of the muscle fibres occurs only in the intercalated discs and therefore the term segmentation is applicable to all such alterations. Fragmentation, meaning separation at points between intercalated discs, does not occur and the term should be discarded.

3. Preliminary to fracture in the intercalated discs they become more prominent than normal. More especially in hypertrophic hearts the prominent intercalated discs are irregular in form.

4. Segmentation depends upon two factors, the condition of the intercalated discs and the tension upon the fibres during

dilatation. If the tension be sufficiently great, segmentation may occur without notable pre-existing lesion of the intercalated discs. Conversely, less tension is necessary if the intercalated discs be weakened.

5. Segmentation may be produced experimentally in rabbits by such marked dilatation as occurs following ligation of the ascending aorta. The change is roughly proportional to the degree of dilatation.

6. A rabbit may survive segmentation for a period of at least 48 hours.

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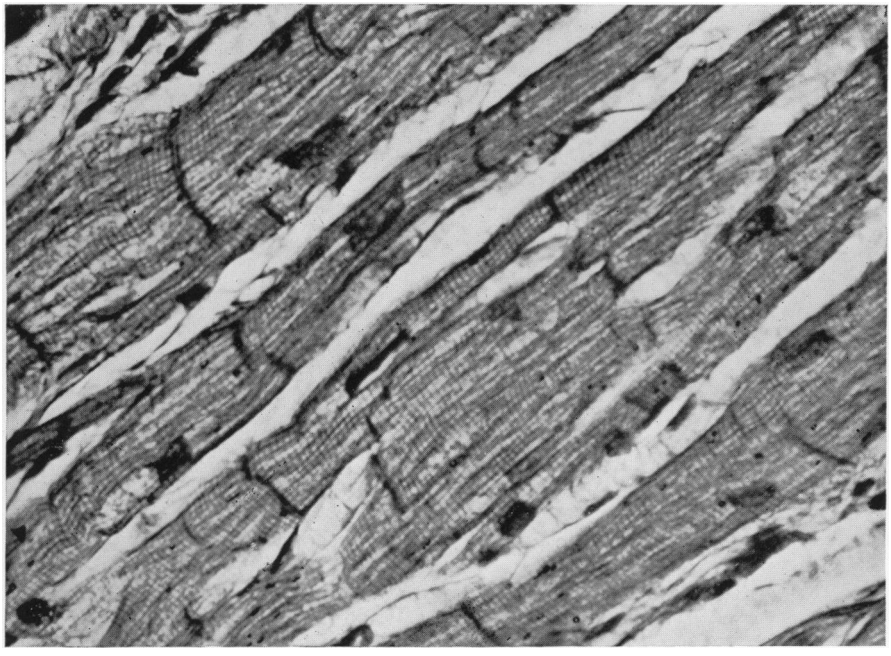
DESCRIPTION OF PLATES LXVIII–LXX

Fig. 1. Conspicuous appearance of the intercalated discs. Hematoxylin-eosin. 4 mm. obj.
Fig. 2. Conspicuous appearance of the intercalated discs. Heidenhain's stain. 4 mm. obj.
Fig. 3. Segmentation in human heart. Hematoxylin-eosin. 8 mm. obj.
Fig. 4. Intercalated discs with comb-form. (After Jordan, see reference No. 51.)
Fig. 5. Segmentation in normal rabbit heart (ligation of arch of aorta). Hematoxylin-eosin. 16 mm. obj.
Fig. 6. Segmentation in normal rabbit heart (ligation of arch of aorta). Hematoxylin-eosin. 4 mm. obj.
Fig. 7. Segmentation in phosphorus rabbit heart (ligation of arch of aorta). Hematoxylin-eosin. 4 mm. obj.
Fig. 8. Segmentation in epinephrin rabbit heart (ligation of arch of aorta). Hematoxylin-eosin. 4 mm. obj.



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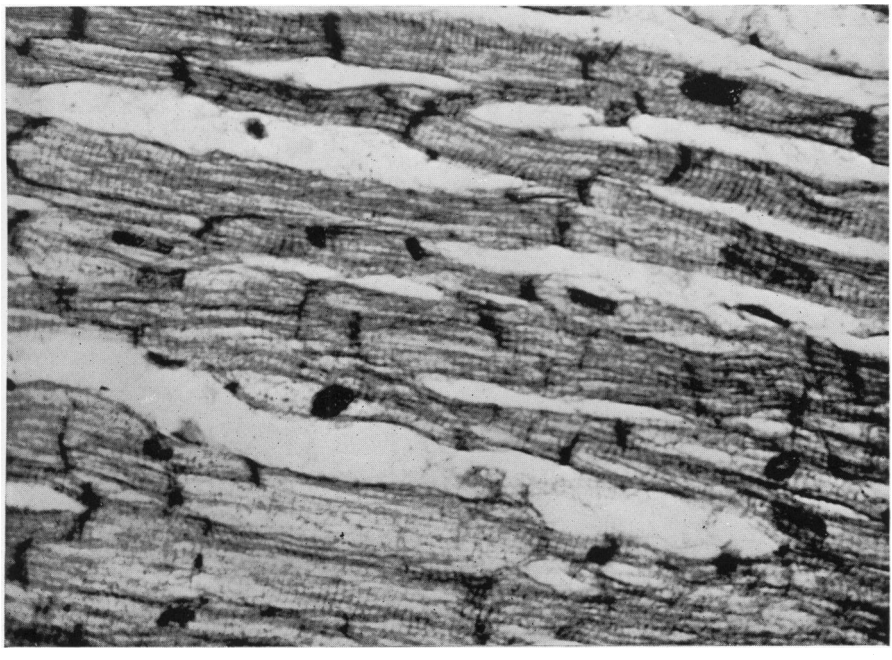

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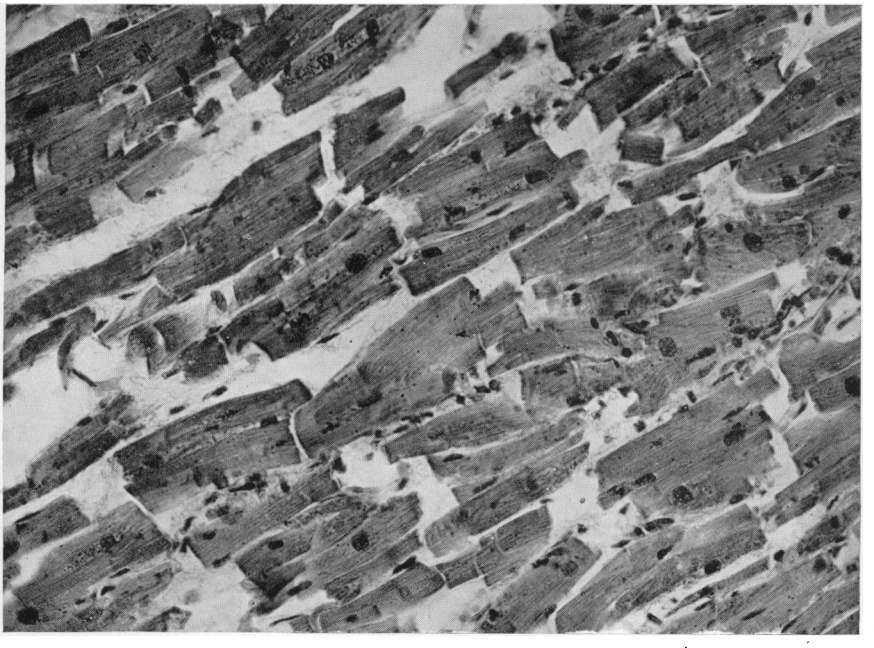

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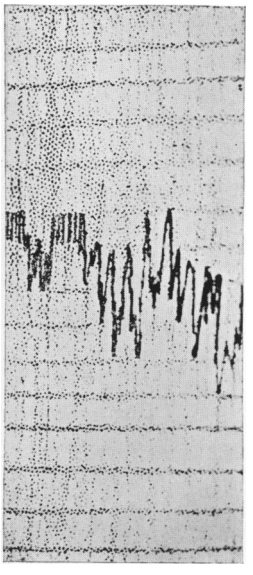

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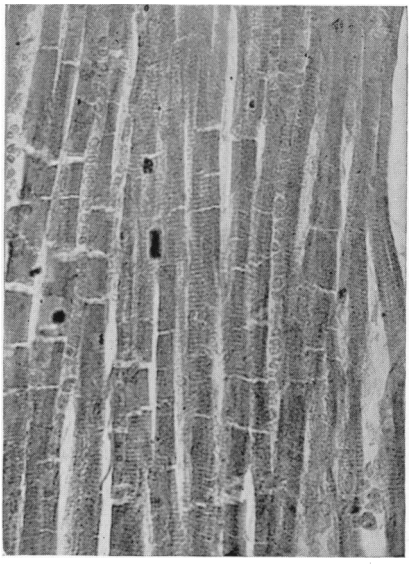

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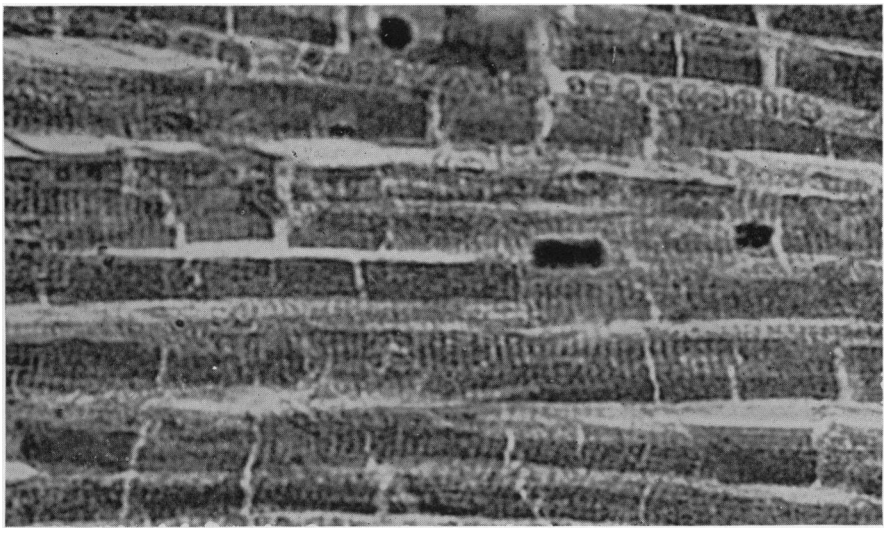

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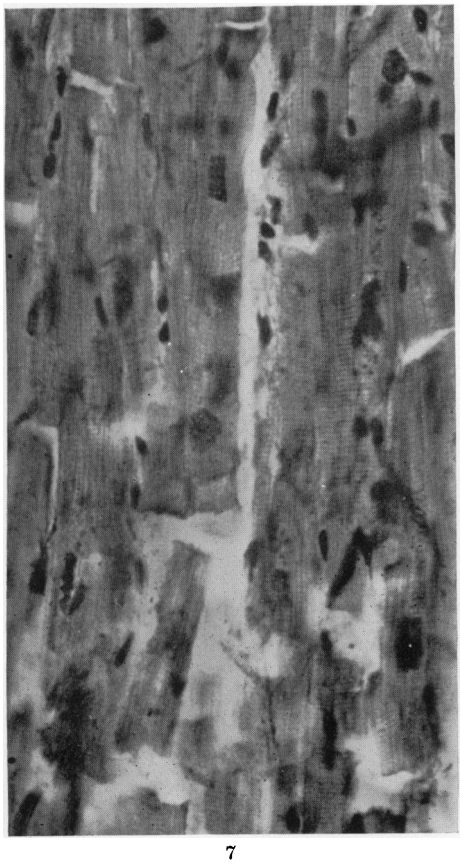

7

8

Saphir and Karsner

Segmentation of the Myocardium