THE SPEED OF HEALING OF MYOCARDIAL INFARCTS.

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Infarction of the heart muscle has been known and described under various designations by pathologists for many decades. The pathological picture in its various stages is quite well known.

Clinical recognition of myocardial infarction, resulting in the main from coronary thrombosis, has been recent, a matter of years and within the memory of all of us. We have set up for ourselves more or less arbitrary rules concerning the average length of time of treatment of patients with myocardial infarction up to the end stage of satisfactory firm scar formation. At the beginning of the period of general clinical recognition of coronary thrombosis ten to fifteen years ago many of us allotted too short a time for bed care and convalescence, at least in some cases. As time has passed we have grown more careful and conservative until now some of us are probably advancing to the opposite extreme of overtreatment with *its* disadvantages. To keep any patient with any disease in bed or at rest too long is not good medical practice; this is especially true in the case of an older person with circulatory disease, because of the need of preventing chronic sluggishness of the circulation with its tendency to promote thrombosis, general weakness, and loss of morale. We may need to take a leaf from the experience of the surgeons who have found that after a minimum period of rest early carefully regulated and graded bodily activity through its various effects on the circulation and well being of their patients speeds the process of repair.

Are we right when we suggest that it is best to keep the patients with uncomplicated myocardial infarction of average severity in bed at *absolute* rest for at least one month, or should the minimum be six weeks, or should it be two months? The same dilemma faces us when we try to decide how long should be the period of convalescence after

the patient has begun to sit up out of bed before he may resume light activity out of doors or take up again a little of his routine work; again we have often but vague ideas or arbitrary rules about a minimum of a month, six weeks, or two months up to a year. There are naturally many exceptions, when complications occur, when the patient's work must be changed or dropped, or when other circumstances arise, but what is the situation from the standpoint of the speed and completeness of healing of the myocardial lesion itself? What clues have we already and can we uncover any more?

Our clinical experience in the last decade in helping to answer this question has been invaluable, but it is still very incomplete. In the first place, we believe naturally and rightly that the larger the infarct the longer it will take to heal. Hence any information that is available about the size of the infarct will help. It is generally, though not always true that the larger the infarct the higher and more protracted is the febrile reaction, the higher the polymorphonuclear leukocytosis, the more rapid and chronic the increased sedimentation rate, the more abnormal the electrocardiogram and the slower its return towards the normal, the more likely is dilatation of the heart with subsequent hypertrophy to occur, and the more often appear serious complications, especially congestive heart failure and rupture of the heart wall. Certain qualifications must be made. A poor state of the coronary circulation in general or in the neighborhood of the infarct, especially common in the older victims, doubtless will delay the speed of healing. The position of the infarct, indicated electrocardiographically in many cases, has been found to be significant; for example, such a lesion at the base of the left ventricle behind the posterior cusp of the mitral valve, due most commonly to acute occlusion of the right coronary artery or of the circumflex branch of the left, is generally smaller and more favorable in prognosis than that in the region of the apex of the left ventricle due commonly to occlusion of the anterior descending branch of the left coronary artery. Presumably the average basal infarct should heal more rapidly than the average apical infarct. Finally, with respect to the healing of damaged heart muscle in cases without heart disease, but with infarction following trauma we have clinically at least increasing information, though still in but a few cases. Our own member, Dr. William

Porter here in Richmond, has had as much or more information concerning this phase of the question as any one I know of. In passing this morning he told me that he thought a period of 8 to 12 weeks might be set for the complete healing of traumatic infarcts. I hope he will say a word about this and refer to any histological examinations that may have been made, as well as of the clinical evidence.*

Do prolonged rest and certain other measures of therapy like the administration of oxygen or theophyllin ethylenediamine hasten healing as we believe they may?

Prolonged and detailed observations along all these lines must be made in the clinic for years to come. But meanwhile we should not miss a very pertinent but much neglected source of information of which I shall speak briefly today, namely, the correlation of the macroscopic and microscopic study of the infarct with its age. It is this study that Dr. Salcedo and I have embarked upon with the essential help of Dr. Kenneth Mallory. We haven't gone far, but I'm sure the idea is a good one and worthy of much amplification. The present note is in the form of a preliminary report.

PRESENT STUDY.

A year ago Dr. Salcedo and I collected the cases of coronary thrombosis examined at the Massachusetts General Hospital or in my own practice who had come to autopsy and who satisfied certain requirements. These requirements were (1) that the date of onset of a typical clinical attack of coronary thrombosis, recent or old, must

*Dr. Porter tells me that he has no histological data concerning the speed of healing of traumatic myocardial infarcts. His most important evidence is electrocardiographic. In one of his cases there was a return of the electrocardiogram to normal in the course of approximately two months or a little more after the injury. The injury in this case consisted of a division of the descending branch of the left circumflex coronary artery with resulting infarction in the left ventricular wall. The electrocardiogram at the beginning showed high origin of the T-waves in Leads 1 and 2, and after two weeks inversion of the T-waves in Leads 1 and 2 for a period of several weeks. The electrocardiogram from a second case with injury from a stab wound in the mid-portion of the anterior wall of the right ventricle showed high origin of the T-waves in Leads 2 and 3 during the first week or two, inversion of the T-waves in all leads one month after the injury, and a return to normal sometime after seven weeks following the injury, but before four months following the injury. One other case of Dr. Porter's showed at autopsy six days after a stab wound of the anterior wall of the right ventricle a healing of the wound, but there was no note of infarction. The electrocardiograms in that case showed nothing of special significance.

be known, (2) that not more than one old attack was clinically recognizable, (3) that a good description of the macroscopic appearance of the infarct and of the heart, or the heart itself, was available, and (4) that there were histological sections of the infarct for Dr. Mallory to study. Quickly we discovered that we had surprisingly few cases which seemed to fill these requirements, only 21 in fact. Hence it was necessary to go elsewhere for help and three other large hospitals in Boston in a most kindly and coöperative way gave us access to their material, 30 cases at the Peter Bent Brigham Hospital, 29 at the Boston City Hospital, and 17 at the Beth Israel Hospital. Thus, from all these institutions we have been able to assemble for our study less than 100 cases, actually 95, and some of these we shall have to discard for one reason or another in our final analysis. The chief defect in our study is at once evident, namely, the scarcity of our cases, and yet that is about the best that Boston can do at the moment.

We have divided all the cases primarily into groups according to the interval of time between the onset of the coronary thrombosis and death. There were 5 patients who died during the first day, 6 during the second day, 7 during the third day, 5 during the fourth day, 5 during the fifth day, 2 during the sixth day, 4 during the seventh day, 22 during the second week, 7 during the third week, 7 during the fourth week, 7 during the second month, only 1 during the third month, only 3 during the fourth month, only 5 during the next eight months, and 9 after one year.

As we would expect, the great majority of the cases were male, 66 in contrast to 20 who were female among the 86 who died less than a year after the onset of the acute coronary occlusion. The average age of the entire group was in the late fifties without much difference among the various sub-groups designated above. The range of age was from 36 years in a patient who died in the fourth month after the onset of the illness to 79 years in a case succumbing during the second week; but patients as young as 42 and 43 died within the first four days and others as old as 71 and 76 survived six months. Many of the deaths were sudden; among the 86 who died during the first year 36 died suddenly, 32 died in congestive heart failure, and the other 18 died of other causes. The majority of the infarcts were lo-

cated in the region of the apex of the left ventricle and were large; this distribution is what we might expect in the more serious cases dying cardiac deaths during the first year and naturally tinges our results. The ratio of the acute infarcts at the apex of the left ventricle to those at the base among the patients dying within the first six months was approximately 10 to 1, and it was of interest that among a considerable number of those dying with acute infarction at the apex of the left ventricle there was an old healed scar at the base of the left ventricle with or without the clinical history of the past occurrence of such a lesion. The infarcts were large in 48 of the 81 cases dying in less than a year with accurate description of the size of the infarct, medium-sized in 25, and small in only 8. Ten of the 86 cases dying within one year showed rupture of the heart wall, 8 had distinct cardiac aneurysms, 47 had intracardiac thrombi overlying the infarcted endocardium (large in 31), and 23 showed acute pericarditis. The heart weights were above normal in nearly all, averaging somewhere about 500 grams in those who died within a year; the increased weight in some of these cases was in part at least attributable to an associated hypertension or to ancient myocardial infarction.

Now we come to the main point of the present preliminary report. Macroscopically the infarct was described as dark red, purplish, brownish red, or dark brown in practically all the cases dying within two to three months of the onset of illness, and as gray or white in those dying later. The weakest part, however, of our whole study to date appears right here, for we had only 6 cases in the very important and critical period between 2 months and 6 months after the onset of the acute illness. We need many new cases in this time interval. It will probably be difficult to get them, for evidently most patients who recover from the acute and subacute stages of myocardial infarction live out at least the rest of the year. We may, however, read into this fact the presumption that to make this possible the healing process after two months must have generally progressed to the stage of a fairly firm scar. We would also like more information about the speed of healing of the small infarcts at the base of the left ventricle. It rather looks as if we must comb the highways

for these among the automobile wrecks or else in hospital and private practice among persons dying of other diseases like pneumonia.

The one other point about the macroscopic character of the myocardial infarct which is of special interest is its consistency. It was almost invariably soft in the first 3 months, but we have only one case in that critical third month. The consistency was hard after 3 or 4 months.

Finally, we come to the microscopic appearance of the infarct and I shall in closing show you some histological sections from infarcts of various ages from our group of cases kindly prepared by Dr. Mallory and loaned to me to show you. Dr. Mallory has made an interesting test in each case by estimating from the appearance of the section the length of time since the beginning of the lesion. He has graded them as follows: 1, represents the reaction and death of the heart muscle cells as the result of the blocking of the blood supply during the first 24 to 48 hours before the appearance of many invading cells; 2, the invasion by multitudes of white cells which come to clear away the debris of the very necrotic myocardium during the first week after the initial 24 to 48 hours; 3, the stage of rapid disappearance of the damaged muscle cells, replacement of polymorphonuclear cells by mononuclears, and new vascularization of the infarct in the second week; 4, the laying down of the scar with the beginning of the appearance of collagen in the third and fourth weeks; and 5, the completely healed scar with much collagen after 2 or 3 months. Dr. Mallory has been able to estimate the age of the infarct quite accurately in this way provided he is given a section from near the periphery of the fresh infarct. He calls attention to the slowness of the progression of the five stages in the center of a large infarct, to the possibility of including an old clinically unrecognized infarct in the section along with or instead of the fresh infarct, and of the fact that often there is a thin layer of surviving heart muscle just under the endocardium kept alive apparently by its close contact with the blood in the ventricular cavity. (Slides shown.)

In conclusion, this study, though much limited in value, especially because of lack of numbers at critical time intervals, supports the clinical impression that fairly complete healing of an uncompli-

cated myocardial infarct of average size may take place in the course of two months.

DISCUSSION.

DR. HERRMAN L. BLUMGART (Boston): I should like to report that there is some corroborative evidence in another direction. Dr. Riseman in my clinic has been studying now for some years the sedimentation rate in all patients with coronary occlusion whom he believes to have cardiac infarction according to the usual signs. The time corresponds quite closely to what one might expect, that is to say, from four to eight or ten weeks the sedimentation rate is elevated, first rising very high and then gradually returning again to a normal level, which is in accord with these studies from an entirely different point of view.

DR. STEWART R. ROBERTS (Atlanta, Ga.): Granting that the infarcted area is of average size and granting that healing is proceeding at the usual rate, what effect would the previous hypertension have upon the prognosis? In other words, to put it more bluntly, in Dr. White's mind would a case of previous normal or low tension have a better prognosis or a worse prognosis than a case of previous hypertension?

DR. CHARLES C. WOLFERTH (Philadelphia, Pa.): Dr. White has contributed a very valuable study on a subject that must be of great importance to all of us who have to deal with heart disease. Our experience has been very similar to that just stated by Dr. Blumgart in regard to sedimentation rate. It varies tremendously from case to case. It is a much more sensitive indicator, I think, of activity than the electrocardiogram, although some rather puzzling electrocardiographic findings may remain a long time that we ordinarily interpret as evidences of activity or of injured muscle.

We have been in the habit of attaching considerable importance to sedimentation rate and placing considerable emphasis upon it in deciding when we think it is safe for our patients to get up.

I should like to ask Dr. White whether he thinks that is a point of any importance.

Finally, on a different type of evidence, namely, electrocardiographic evidence, my associates and I concluded that anterior infarcts were of much greater import than posterior, and I am naturally very much interested to find that on this type of evidence Dr. White has apparently come to a similar conclusion.

DR. DAVID FARLEY (Philadelphia, Pa.): My remarks are stimulated more by those of Dr. Wolferth and Dr. Blumgart than of Dr. White. Perhaps that is not fair. I should like to put in a plea for the nuclear count as of possible use in these cases rather than the sedimentation rate.

DR. PAUL D. WHITE (Boston): I am afraid I cannot answer with statistics Dr. Roberts' question about the effect of previous hypertension, but it is my impression, and I think it is that of many of us, that the patients who have had prolonged hypertension with large hearts have done less well when infarction comes than those cases with normal sized hearts without previous hypertension, but I think that if hypertension has not left much enlargement of the heart it

may be a different matter. My experience is certainly that, and it is theoretically to be considered a probability that previous hypertension with enlargement of the heart should make the prognosis less favorable.

I have very little information myself on sedimentation rate. I am sure that it is an important lead to follow and it may possibly be clinically the most important of all after other evidence has subsided, but we must remember constantly that complications may intervene to color the picture. I wonder even whether intracardiac thrombus in the process of organization (I don't know how long it takes an intracardiac thrombus to organize) might alter the sedimentation rate.

SUMMARY OF TWENTY CASES OF

TUBERCULOSIS OF THE PERICARDIUM.

Case No.	Symptoms	Physical Signs						ema	Fever	W.B.C.	Duration of Illness	Anatomical	Remarks		
		Size of Heart (cm.)	Friction Rub	Pericardial Fluid	Murmurs	Arrhythmias	B.P. Systolic/Diastolic								
WASTING DISEASES								TH OBSCURE FEVER.							
1.	Progressive weakness 2 mos. Loss of weight. Constriction across chest 6 wks. 70 ♂	10 x 7	+	0	0	Feeble breath sounds	0	144/66	100°-103°	5,900	3 mos.	Tbc. lymph nodes; tbc. pericarditis.			
2.	Loss of weight; weakness; fever; mental confusion. 72 ♂	12 x 3	0	0	0	0	0	130/88	99°-100.4°	16,500	?	Tbc. pericarditis; tbc. lymphadenitis; tracheo-bronchial lymph nodes; chronic tbc. with cavity.			
3.	Loss of weight; weakness; fever. 71 ♂	12 x 3	0	0	0	0	?	?	Normal 101°-102.8°	18,000-20,000	4½ wks. on ward				
4.	Fever; loss of weight and weakness. 60 ♀	13 x 3	0	0	0	0	111/78	0	100°-102°	19,600	?	Tbc. epididymus; miliary tbc.; obliterative fibrosis; pericarditis with calcification.	Miliary tbc.		
HEART FAILURE WITH CONGESTION.															
5.	Dyspnea 10 months. Edema of legs 5 mos. 63 ♂	11.5 x 3	0	0	0	Sounds distant	0	90/30	+	Generalized	0	8,200	10 mos.	Adherent pericardium; tbc. pericarditis; right hydrothorax; miliary tbc. of lungs; ascites; C.P.C. of liver and viscera.	Progressive heart failure; terminal miliary tbc.; afebrile; cyanosis striking.
6.	Constriction in chest 2 mos. Shortness of breath 2 mos. Edema of legs 6 wks. 60 ♂	12 x 4	0	0	0	Sounds distant	0	135/90	+	Generalized	0	11,000	2 mos.	Tbc. bronchial and mediastinal lymph nodes; tbc. pericardium and pleurisy; hypertrophy of heart; hydrothorax; ascites.	Progressive heart failure, onset suggesting pericardial or coronary artery disease.
7.	Pain in chest and abdomen 1 mo. Cough 1 mo. Abnormal swelling 3 wks. 22 ♂	14 x 5	0	0	0	0	115/70	0	99°-103°	12,000	2 mos.	Tbc. bronchial and mediastinal; tbc. pericarditis; dilatation of heart; C.P.C. of viscera.	Great cardiac enlargement. Pericardium varied from 2.5 to 3.5 cm. in thickness at necropsy. Miliary tbc.		
8.	Pain in chest and abdomen 5 mos. Shortness of breath 3 mos. Edema 1 mo. Precordial pain 1 mo. 26 ♂	12 x 4	0	0	0	0	110/60	+	Generalized	97°-100.4°	10,000	5 mos.	Tbc. pericardium; tbc. bronchial lymph nodes; miliary tbc. of lungs, pleura, spleen, liver; ascites and bilateral hydrothorax.	Febrile illness at onset followed by heart failure within 3 months.	
9.	Pain in chest. Dyspnoea; cough; swelling of abdomen and feet. 43 ♂	12 x 3	0	0	0	Sounds distant	0	110/80	+	Dependent	99°-102°	4,250	2½ mos.	Tbc. of bronchial and mediastinal lymph nodes; tbc. pericarditis; C.P.C. of viscera.	
10.	Failing health for 1 yr. Dyspnoea and constriction across chest 2 mos. Cough 2 mos. 81 ♂	11 x 4	+	0	0	Faint heart sounds	105/75	+	99°-101°	7,400-14,000	1 yr.	Tbc. pericarditis; tbc. of pleura — bilateral; tbc. tracheobronchial nodes.			
11.	Pain in epigastrium and upper part of left scapular region 2 mos. Dyspnoea 2 wks. Edema 2 wks. 50 ♂	12 x 4	0	0	0	Auricular tachycardia with partial heart block and dropped beats	134/110	Dependent	0	5,200	2 mos.	Tbc. pericarditis; obstructive pleuritis; left hydrothorax; tbc. of bronchial and mediastinal nodes.			
12.	General malaise for 3 mos. Edema of extremities 2 mos. Dyspnoea on exertion. Orthopnoea. 74 ♂	13 x 4	0	+	Faint heart sounds	Sino-auricular tachycardia. Left ventricular preponderance	110/95	+	Dependent	98.6°-101°	4,500	5 mos.	Tbc. pericarditis with effusion (300 c.c.); coronary arteriosclerosis; C.P.C. of viscera.	Miliary tbc.	
PERICARDIAL EFFUSION.															
13.	Pain in chest 1 mo. 24 ♀	13.5 x 4	+	+	0	Faint heart sounds	105/75	0	99°-101°	4,200	6 mos.		Recovered.		
14.	Pain and constriction in chest 1 mo. Dyspnoea 1 mo. Loss of weight. 49 ♂	15 x 7	0	+	Tapped twice	Soft systolic at apex	126/87	0	99°-101°	12,600	1 mo.	Pericarditis with effusion; tbc. of mediastinal lymph nodes; pleurisy with effusion.	Pericardial cavity contained 3500 c.c. at necropsy.		
15.	Pain in left chest 2 wks. Dyspnoea 2 wks. Edema of legs 2 wks. 70 ♂	13 x 4	+	+	Aspirated 3 times, 2100 c.c. removed	Faint heart sounds	110/80	+	Dependent	0-100°-101-102°	6,500	3½ mos.	Tbc. pericarditis with effusion; miliary tbc.; pleural effusion, left.		
16.	Shortness of breath; pain in chest. 22 ♂	12 x 4	+	+	0	0	110/70	0	100°-101°	9,600	3 mos.		Recovered. Dextrocardia.		
17.	Fever; abdominal distention. 52 ♂	10.5 x 9	0	+	0	0	115/90-95/80	+	Ascites	99°-101°	9,000	7 mos.		Tbc. peritoneum; tbc. pericardium with effusion; cirrhosis of liver?	
TERMINAL.															
18.	Sense of constriction across chest 3 mos. 46 ♂	14 x 3	0	0	0	0	220/118	+	99°	14,400	3 mos.	Tbc. pericarditis; tbc. mediastinitis; chronic nephritis.	Terminal in hypertension with chronic nephritis.		
19.	Nausea and vomiting 3 wks. Ascites 2 wks. 55 ♂	12 x 3	0	0	0	+	Auricular fibrillation	80/50	+	Dependent	98°-101°	4,000-15,000	7 wks.	Tbc. pericarditis.	Terminal in cirrhosis of liver.
20.	Weakness and dyspnoea 3 wks. 70 ♀	11 x 3	0	0	0	Auricular fibrillation	105/65	0	98.6°-99.2°	12,500	3 wks. +	Tbc. pericarditis; cirrhosis of liver; pulmonary tbc.	Terminal in cirrhosis of liver.		