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# Coronary artery disease with myocardial infarction : historical review of the present status with a review of some of the recent literature

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# CORONARY ARTERY DISEASE WITH MYOCARDIAL INFARCTION; HISTORICAL REVIEW OF THE PRESENT STATUS WITH A REVIEW OF SOME OF THE RECENT LITERATURE

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TABLE OF CONTENTS

## INTRODUCTIONARY NOTE

It is not the purpose of this paper to discuss the field of coronary artery disease, but to limit the subject to coronary conditions with myocardial infaretion. An attempt is made to form a summary of the accumulated information upon a subject of vital and increasing importance. This attempt is probably justified from the fact that in recent years the conviction has been growing that the incidence of coronary heart disease the world over has been continually increasing ($\frac{55}{56}$) and that physicians are among the most frequent victims. (57,58,59)

## GENERAL CONSIDERATIONS AND HISTORICAL REVIEW

The historical development of the knowledge concerning clinical recognization of coronary thrombosis forms an interesting chapter of modern internal medicine. Despite the fact that most cases can be readily diagnosed, it is only of recent years that its distinctive features have been properly understood, and differentiated from those that pertain to allied but decidedly different morbid states. The bulk of our knowledge has come thru careful observation of practicing clinicians together with the usual examination of their postmortem material rather than experimental investigation. (1)

The throb of the heart and the beat of the pulse have long been known, and probably no mechanism in the entire mammalian structure has arroused greater speculative interest, awe and reverence than the orderly beating heart. For 1400 years knowledge of the heart function and its diseases rested in the bosom of ignorance and on the preposterous concepts of Galen and his many disciples. The influence of Aristotle, Praxageras, Erasistratus, and Hippocrates was but a momentary rift in the clouds of misconception. Galen said,"The heart is as it were a lamp or light in the middle of the body blood being the oil that feeds the flame, and the inbreathed air that keeps it burning. Respiration, there-

fore, is to keep the flame of the heart alive and to engender the vital spirits." Though Galen was wrong so many times, it was he who first ascribed the symptom of palpitation to cardiac malfunction, yet for many years thereafter the heart was rarely accused of any symptoms. One of the earliest allusions to pectoris delor was made by Bonetus in 1679, there is not a word on the cardiac pain or disease of the coronary arteries. With the unconscious modesty born of true greatness, William Heberden, in 1768 penned his immortal symptom-complex, "Angina Pectoris", and even he was totally oblivious to the fact that these chest pains might have been due to changes in the coronary arteries. He published his observations with a description of a case we know now as an instance of true coronary occlusion rather than on of angina pectoris. Heberden felt that angina pectoris was caused by spasm and unrelated to inflammation, yet he dared not venture a guess as to where the site or the spasm was. Strangely it remained for Jenner, to discover the connection between coronary sclerosis and angina pectoris. Though Jenner made this discovery in 1772, he did not announce it until 1799, out of regard for his friend, John Hunter, whom he did not wish to alarm and who was suffering unmistakable symptoms of angina pectoris at the time. Because of such devotion to

a friend, he lost priority in the literature, and it was Black who published the connection between angina pectoris and coronary sclerosis in 1795. However, Jenner's description of the autopsy which caused him to subscribe to the theory of coronary change is very interesting and worth quoting:

"I was making a transverse section of the heart near its base, when my knife struck against something so hard and gritty as to notch it. I well remember looking up to the ceiling, which was old and crumbling, conceiving that some plaster had fallen down. But on further scrutiny the real cause appeared; the coronaries were become bony canals."

Parry and Fothergill also subscribed to Jenner's ideas; in fact Parry, who in 1799, first subscribed the theory of ischemia of the heart muscle as the chief cause of anginal pain. Since then, the argument has raged unabated; even such men as Allbut, Wenekebah and Vaquez stuck tenaciously to the aortic theory of pain. They were anticipated by Burns who wrote in 1808 and Kreysig in 1814, stressing the coronary artery theory of angina pectoris.(2) A glance at a few works published before 1880 will show the varied reactions of this theory and the uncertain status of the coronary artery. Allan Burns, the young Blasgow anatomist and surgeon

who, at the time of his early death at thirty-one, gave promise of adding lustre to British medicine, published in 1809 his volume on diseases of the heart. He adopted the coronary artery theory of angina pectoris, especially as promulgated by Parry, and aimed to corraborate it by experiment of the ligatured limb. This seems to have been the first recorded experiment that tried to prove the nature of anginal pain.

In Germany a translation of Burns on the heart was published in 1813. In 1814 Kreysig brought out his lst volume on the heart. He criticized rather freely other writers for the narrowness of their views concerning affects of the heart in general. He destinctly recognized the importance of the coronary artery and raps on the knunkles of those who question the existance of angina pectoris. He is familiar with the works of Corvisart, Burns and Testa, the latter who in Italy had in 1810 written a three volume works and devoted several pages to angina. He also accepted the coronary artery theory with reservations; for, as seen at autopsy, there were many cases of marked ossification of the arteries with no anginal symptoms during life. The most popular book on the heart of early nineteenth century was volume by Corvisart, but neither of editions in 1806 or 1818 contained anything definite concerning angina pect-

oris and only casually mentioned the arteries. Nor did Laennec in 1819 give more than scant attention to angina pectoris or coronary arteries. Bovilland in 1835 quotes with approval Laennec's statement, "Many patients are met with experiences of constant or interval pains like those of rheumatism and neuralgia, referring them to the heart, pains which the patients and often the doctors wrongly attribute to an organic affection." Bovillard then discusses these briefly under the head of neurosis. It seems highly probable that some of these pains described by Laennec, especially those that occured "at intervals" were of coronary origin. (1) Then followed another school of thought by Corvisart, Laennec and Stokes and Hope, who felt that angina pectoris was to be explained on a nervous basis. (2) The tendency to magnify the influence of the nerves and to minimize or overlook that of the artery and muscle was not confined entirely to the French clinicians. Both Hope and Stokes were of this opinion. Even as late as 1868, von Dusch spoke of angina pectoris as a rare condition stating that in Hamburg 1845 there were three fatal cases in a total of 5171 deaths of all causes. He favored the view that the cause of the disease was inflammation of the cardiac nerve plexus.

About the middle of the nineteenth century, exper-

imental investigation became more active. "Myomalacia Cordis" was made popular by Ziegler. It was now recognized that obstruction of the coronary arteries was a frequent case of those degenerative necrotic, or atrophic processes that later led to smaller or larger areas of fibrosis to which macular weakness, dilation and cardiac inefficiency were often due. The designation "Chronic myocarditis" is still employed, though not regarded as appropriated terminology by which to d esignate all such scar like areas or their mode of origin. The importance of the muscle and not alone the valves was dwelt on by Krehl, a view late revived and energetically preached by Mackenzie. (8) Cohnheims experiments in dogs supported the idea that the acute obstruction of the coronary artery was generally fatal and the arteries were endarteries. Other men coundn't support him as their animals lived for days. The end results of coronary occlusion were set forth in two excellent studies, one by R. Marie 1896 and Maximalian Sternberg in 1914. In these works the two conditions, parietal aneurysm and myocardial infarct, were clearly recognized as due to coronary occlusion, yet both were too intent on the pathology and result of the infarct to notice plain and destinct tell tail symptoms marking the time when the acute blocking had taken place. (1)

Although these findings and arguments arose, more than a century passed before anyone recognized the symptomatology of coronary occlusion whth myocardial infarction. Isolated cases had been reported by Leyden in 1884 and even diagnosed by Hammer in 1878, and it is now easy to wonder why coronary occlusion, long recognized pathologically, had not been correlated earlier with its clinical picture. It was in 1910, that two russian physicians, Obrastzow and Straschesko, described the clinical aspects of coronary occlusion; their word was ignored. In 1912, our own Herrick (5) published a splendid paper, discussing in detail the symptoms, signs and pathology of coronary occlusion, only to find himself a prophet in the absolute wilderness of conservatism and stagnation, no one paying any heed to his work except Libman, It was not till 1919, after many lectures and another paper by Herrick, (9) that the profession awoke. Head and Mackenzie (8) helped our understanding as to why we found at times cases of marked coronary sclerosis without anginal symptoms, and vice versa, by stressing the factors of individual sensitivity to pain determining the severity of the symptoms. In this country, especially, there has been much work on the subject of coronary artery disease, in an effort to prolong life through its earlier recognition; papers by Riesman and

others on myocardosis are worthy of mention. (2)

For a great many years both clinicians and pathologists were observing rupture of the heart, aneurism of the ventricle, occlusion of the coronary arteries and myomalacia, only as a pathological process without recognizing any clinical value because they were thought to be unrecognizable during life. In fact it was not generally appreciated that occlusion of the coronary arteries could be compatable with fair degrees of health. What we now recognize as acute thrombosis was regarded as angina pectoris or Status Anginosus. It is this distinction that is a development of the past 15 years. (3) Until a few years ago, Sir Wm Osler in his Lumelian Lectures (4) divided angina pectoris into types: (mildest, mild and severe). The severe ones were evidently thrombosis. There was no clinical antemortem differentiation being made between contitions of coronary thrombosis and angina. The same may be said of James MacKenzie in his work published in 1924. (8) He has not made clinical diagnosis of coronary thrombosis in his practice. Two other names connected with the literature on coronary thrombosis are Krehl and Huchard. Krehl called attention to possible recovery after an attack and also discussed aneurism and ultimate rupture of the ventricle. Huchard in a pathological analysis of 185

cases of fatal angina, called attention to the frequency of coronary thrombosis. Dock was on of the first to report instances of coronary thrombosis diagnosed antemortem and proved at autopsy, and recognized the importance of precordial friction rub as an aid to diagnosis.

The first important and satisfactory account of the clinical features was published by Obratzow and Strascheske who diagnosed 2 out of 3 cases and emphasized a triad of symptoms as severe lasting retrosternal pain, dyspnea, orthopnea and gastralgia. All 3 had precedent angina. Also they called attention to gallop rhythm, cheyne-stokes breathing, pericardial friction, distant heart sounds and also different clinical and pathological events resulting from the size of the coronary artery involved. They also recognized that softening and rupture of the infarcted area might result with hemopericardium, describing fever when present. Hochhaus diagnosed two more cases antimortemly.

During the last 15 years physicians in America have added much to our knowledge concerning this condition. Herrick (5) focused the attention of American medical profession on this disease and to him belongs credit for the present concept of coronary artery thrombosis. In 1912, he emphasized during life that it need

not end fatally. The same year his second article appeared.(9) Levine and Tranter(6) published a report of two cases of coronary thrombosis, one diagnosed antemortemly. During this time it was quite clear that Libman has been familiar with coronary thrombosis as a condition differing from ordinary attacks of angina. In 1916 (7) he mentioned, "the diagnosis of a recent thrombosis could often be facilitated by development of a slight temperature or a moderate leucocytosis and evidence of a patch of pericarditis all within a couple of days after an attack of severe pain. Levine and Tranter(6) were the first to call direct attention to the development of fever and leucocytosis as a part of coronary thrombosis and showed the relationship to acute upper abdomenal conditions. Gorham, pointed out the diagnostic importance of pericardial friction rub and its frequency while Wearn (10) besides giving clear descriptions of the signs and symptoms of the disease, called attention to a marked diminution in the height of the EKG waves. Levine brought out the fact that those who had had hypertension and angina before the attack of coronary thrombosis might be free of anginal attacks if the attack was attended with permanent and and distinct lowering of the blood pressure.

Not until 1925, did the subject of coronary throm-

bosis become a specific problem in England. Allbutt called attention to the pathological condition so far as it affected his theory of aortic origin of angina. Mackenzie maintained the importance of the blood supply to the heart in the mechanism of the attacks.

A most important and helpful advance in the clinical recognition of coronary thrombosis came about in this country when certain EKG changes were found to be fairly characteristic of the acute stages of this condition. Smith noted sharp inversion of the T wave on EKG in the dog, shortly after the coronary arteries were ligated.(1) At about this time, Herrick published an account of the first coronary thrombosis which was proven by post mortem examination with the EKG showing sharp inversion of the T waves in lead I and II similar to Smiths. He also noted the T waves were less negative 10 days later, in 5 month tracings, curves of low amplitude were produced. The discovery of Pardee that there are instances in which this EKG sing may be the single evidence that distinguish the condition and differentiate it from unrelated possibilities like gall stones or gastric ulcer. These changes are described as high take off of T wave from descending limb of the R wave. This does away with the RT interval. It was also noted that the T wave becomes inverted.

Rothschild, Mann and Oppenheimer found the characteristic changes in the RT interval as soon as 6½ hours after the onset of the attack.(1)

And so, though the start was slow, and jogging, along the same old ruts that had to be overcome, we have finally become sensatized to this subject and our clinical advances have been quite rapid.(2)

## INCIDENCE AND ETIOLOGY

Myocardial infarction occurs most frequently between the ages of fifty and seventy years. It is not uncommon between forty and fifty and seventy years but is rare below forty. It is two to three times as common in men as women. Thrombosis is especially common in persons who have had the anginal syndrome. Coronary embolism is rare.(12)

Diseases of the coronary arteries are divided into angina pectoris and coronary thrombosis. These conditions have much in common, and also many divergent points in etiology, pathology, prognosis and treatment. Briefly the former is due to a temporary inadequacy of coronary blood supply while the latter is caused by a permanent obstruction. The resulting effects in the myocardium differ between a temporary ischemia and destruction of its fibers.(13)

Among the contributing factors prolonged mental strain is frequently emphasized. White lays emphasis on the stress and speed of modern life as an etiological factor. Newspaper reports of frequent sudden deaths seem to corraborate this contention. It has more or less been accepted that "brain workers at high tension" are particularly liable, but Boss and Donner report that the incidence in the working classes is as high,

and that the disease is more malignant. Herrick believes that the condition, like cancer, has an apparent increase partly due to the fact that larger numbers reach the senescent years. The all important disease of these vessels is arteriosclerosis. It is by far the chief cause of angina pectoris and coronary thrombosis. In the former it may often elude the gross inspection, but may be demonstrated by the injection of arteries by microscopic studies. In the latter it is prictically always present. Parkingson, Herrick, Marie, and Ashoff all attribute the major. if not the sole role to arteriosclerosis.(13) Occlusion of the coronary artery may result from one of several lesions or combinations of them: 1. Thrombosis, 2. Intramural coronary artery hemorrhage, 3.Severe arteriosclerosis with stenosis, 4. Syphilitic aortitis and coronary arteritis with narrowing of the ostia, 5. End arteritis, 6. Embolism. The most common in cause is thrombosis of the coronary artery at the seat of severe partially occluding sclerosis. Intramural coronary artery hemorrhage is probably secmost common cause. Careful study shows that many coronary arteries are occluded by massive hemorrhage into the vessel walls and from large hematoma which block the lumen by the size or rupture of the intima and thrombus formation.(18)

## Arteriosclerosis

Horn and Finkelstein(15) maintain that coronary occlusion is incidental in arteriosclerosis. Arteriosclerosis was noted in every instance of partial or complete arterial occlusion. In not a single instance was a thrombus present within a normal artery. Master, Dack and Jaffe also found coronary sclerosis as the underlying pathologic condition of coronary occlusion.(34) It is increased with work of the heart. Professional groups show it more than manual laborers. The florid robust type of person has coronary sclerosis while the asthenic type has the disease only rarely. (23) The relative incidence and degree of coronary atherosclerosis is significantly higher in private patients than in the general wards. In the middle aged group this incidence was twice as much.(25) Arteriosclerosis is generally agreed to be the underlying cause of coronary thrombosis of the coronary artery. The exact mechanism is unknown. Several hypothesis have been advanced but stagnation or eddying of blood following stenosis of the lumen by arteriosclerotic plaques may cause the condition.(17)

## Intimal Hemorrhage and Hypertension

It is shown that increased capillary pressure due to hypertension is the major factor in the formation of

production of intimal hemorrhage.(14) Intimal hemorrhage in the coronary arteries is the usual fore-runner of thrombosis and occlusion. It is the end result of a progressive degenerative arteriosclerotic process and is probably a fortuitous event.(16) Horn and Finkelstein feel that arteriosclerosis is a sequela rather than the basis cause of intimal degenerative changes. Intramural hemorrhage is found in association with vascularization and plaque degeneration and originates in the wall with imbibition of the lumen. Coronary occlusion can be caused by intramural hemorrhage in (62.5%) and by thrombosis of an arteriosclerotic plaque in (37.5%). They also noticed that in every case of coronary artery occlusion, arteriosclerosis was noted. In not a single instance was thrombosis present in a normal artery.(15) Patterson finds the microscopic observation suggests strongly that intimal hemorrhage is intimately concerned with the etiology of coronary thrombosis.(14) Capillary rupture may initiate thrombosis of the coronary arteries by the diffusion of

blood into the lumen, by necrosis or erosion of the intima from dammage to capillary circulation or by retrograde capillary thrombosis. This work was confirmed by W.S. Wartman.(18)

Hypertension is the outstanding etiological factor in the production of coronary sclerosis.(20) The association of hypertension and diabetes appears only to bear a relationship comparable to the predominate age period represented by the group of patients in study.(26) Coronary sclerosis is rare in both sexes without hupertension.(19) Master, Dack and Simon found in their series that half the men and four fifths of the women showed hypertension increasing with age at 30% at 40 years to 74% at 70 years , but the mortality was unaffected. Hypertension is definitely an etiologic agent for its incidence in coronary sclerosis is definitely greater than it is in the general population and the ratio of the attacks in the hypertensive male is 5 to 8 times that of the normal male although both groups increase with age. Hypertension increases the aging process.(36) In women, coronary disease seldom occurs except in the presence of hypertension or diabetes,(26) but despite the slightly higher frequency of hypertension in women, the incidence of coronary disease is only three fourths that of men.(1,41,26) This latter circumstance to some

extent impairs the significance of hypertension as a cause of coronary disease.(40)

Race and Sex

During the four year period of 1931 to 1934, the death rate for white industrial policy holders of the Metropolitan Life Insurance Co. from coronary disease among males was found by L.I.Dublin to be 16 per 100, 000 as compared to 3.5 among the females in ages 35 to 40. The rate for males was four times that of the females in the age period of 45 to 64 and two and ½ times that of the female in 65 to 74 age period. When coronary disease was particularly significant as a cause of death, the mortality was 173.6 in males; almost double the rate 93.7 in females.(42) Clawson found the incidence in males predominates with a ratio of 2.5 to 1,(20) while Baker and Williams found the infrequency ratio in women of 7 to 1, and it occurs later in life in women as shown by the fact that in the ages of 50 to 80, coronary thrombosis occured 89% women and 79% men in that age; occuring 6 years later in life in women, and along with this they are less susceptable to coronary thrombosis.(26) Master, Dack and Simon found the ratio to be 3.4 to 1, men having the greater incidence. The average age of women was higher than men with the incidence in women rare under 40.(36) Race--Weiss(19)

ance of fat metabolism. The high frequency of coronary disease is illustrated by Joslins experience.(43) In an analysis by the Metropolitan Life Insurance Co of deaths among the diabetic patients, coronary disease accounted for 139 deaths or 14.2% of all deaths between Jan. 1930 and March 1935. The frequency of coronary disease in diabetics is confirmed by the figures of Levine(3) and Conner and Holt.(44) Necropsy studies also afford a good evidence of the high frequency of coronary arteriosclerosis in diabetes. Warren in his study of 270 cases of diabetics, at necropsy found sclerosis of the coronary artery in 124 with 52 marked cases. (45) Nathanson in his series of 100 diabetics found coronary sclerosis in 41 cases.(46) Fitz and Murphy called attention to the great frequency with which diabetics died of vascular disease. This particularly is true of diabetic patients over 35 or 40 years of age; at any age when the diabetes is not particularly severe.(47) The fact that the presence of diabetes did not alter the prognosis of the attacks of coronary thrombosis or the age at which they occured, leads one to feel that it had no causative influence in the disease, but melely indicates the type of person who has a vulnerable vascular system.(42)

Syphilis

Levine(1) has shown in his series of 89 patients with coronary thrombosis, there were only 3 with a posative Wasserman and 1 that gave a history of primary syphilis and only 4.5 were syphilitic. White and Bland (48) found in 200 cases that 96% were Wasserman negative and Conner and Holt found 14.2% in 247 cases.(44) Levy likewise consluded that Syphisis is not more common in coronary disease than in any other unselected group. His findings were 13.4% incidence of Syphilis. Applebaum and Nicolsons series of 168 cases of occlusive diseases of the coronary, found syphilis in 10 patients, 9 of whom occlusion of one or more coronary orfices was caused by luetic processes in the aorta. They say "It is important to note that pathologists do not regard syphilis as an etiologic factor in the production of arteriosclerosis."(1) Kessane, Koons, Mahanna in 5,859 cases at autopsy, divided into syphilitic and non-syphilitic cases, showed that coronary artery sclerosis was four times more common in the syphilitic group. In conclusion it is evident that syphilis is not a primary or secondary factor in the production of coronary artery occlusion or angina.(28) Syphilitic aortitis may be the indirect source of embolus as cited in the 3 cases by Porter and Vaughan.(27) Special lesions are often encountered involving the coronary

arteries such as Buergers disease and syphilis. The latter may in rare instances produce a diffuse arteritis affecting the larger or smaller coronary arteries. Mahar, Warthm (49) and von Glahn (50) noted the process is apt to affect those arteries above the area where the syphilitic process in the aorta usually ceases.

Body Build and Heredity

The constitutional type described by Levine(1), the well set stocky strong man with rounded forearms appears to be the type most apt to develop coronary sclerosis and angina. Coronary disease afflicts the overweight much more frequently than those of slighter build. This was likewise indicated by the frequency in diabetics who are generally overweight.(42) Dublin and Marks(52) in 200,000 men insured by the Union Central Life Ins. Co. found death rates due to coronary and arterial disease high among the overweights. The death rate from angina was 2 times more in persons overweight than normal and 2½ times those underweight. There is as yet insufficient evidence of relation of heredity to coronary disease. In Levine's series(1) of 145 patients with coronary thrombosis, many gave a family history of familial susceptability to vascular disease. This was especiall true among younger patients with coronary disease.

## Occupation and Age

Professional groups and white collar groups show coronary disease more than manual laborers in Bähr's experience. In so far as available, figures indicate occupation is not an important factor in the incidence of coronary disease although the prevailing impression has been very much to the contrary. It has been assumed that the increasingly rapid pace of modern life was to be blamed with increasing heavy toll taken of such high-powered executives, business leaders, physicians and other professional workers who suffered from the strains of intense activity. Levy's figures do not confirm these surmises.(51) They show that the largest percentage of coronary disease cases was among foreman and skilled workers. Until mor evidence is accumulated it is well to follow the clue that and increased incidence reflects largely the rising average age of the population plus changes in the medical practice and fashions in diagnosis.(42) In 500 consecutive cases two thirds of the attacks were between the ages of 45 and 65. One third before 50, with the peak in the sixth decade. The number of progressive attacks rose till the age of 45 then a level till 64, after which was a decline. It was extremely rare in groups 27 to 39, as shown by Master, Dack and Jaffe.(36)

## Activity

Levy(25) noted in 1,440 cases that occupation and social status did not predispose to coronary artery occlusion. It occured in sleep 22.2%, rest 31.1%, in mild activity 20.2%, moderate activity 8.5%, walking 15.8% and unusual exertion 2.0%. With the exception of surgical proceedures, meals, emotion and excitement or infection, trauma did not play a part in the etiology. Sixty patients suffered an attack following being bedridden for weeks or months for chronic illness. The time of the attacks was well distributed through the day with peaks at 2 AM and 10 PM to show activity is not a great factor. He feels there is no evidence in his series to show that physical effort or excitement produces intimal hemorrhage in the coronary arteries which is the usual fore-runner of thrombosis and occlusion. Intimal hemorrhage is the end result of a progressive degenerative arteriosclerotic process and is probably a fortuitous event. It was found at necropsy as frequently in bed-ridden patients as those with marked physical activity.(25) Bähr showed that professional groups were afflicted as often as were manual laborers.(23) Patterson(17) feels that coronary artery capillary walls may rupture in the arteriosclerotic plaques producing intimal hemorrhage and

coronary thrombosis because of a trantient rise in blood pressure which accompanies exertion or excitement. He also thinks one should advise against excessive excitement, emotion or activity if coronary disease is known to exist, to prevent undue rise in the intra-capillary pressure. (17)

Other Factors Of Etiology Mentioned

Xanthomatosis--Müller(37) believed Xanthomotosis to be the dominent factor in 17 cases of families with hereditary heart disease. The patient gives rise to special forms of arteriosclerosis. Its deposites may cause valvular lesions, but far more the changes may be in the coronary arteries causing angina or infarction of myocardial structures frequently. Hypercholesterolemia was present with xanthomatous deposites in the skin. Heart disease in families direct attention to xanthomatosis when rheumatic fever, lues, and hypertension fail to play a part.

Environment--Bean and Mills(39) support the contention first mentioned by Wolff and White in 1926 that most of coronary thrombosis cases occured in the winter between october and april. Conronary occlusion attacks are definitely more common in winter than summer. In the north temperate regions studied there was a greater frequency of infection and increase in general body

metabolism probably acting together to increase winter hazards for the cardiac patients while the calm and warmth bring a period of relative safety.

Embolism--In 3 cases in 12,000 autopsies, death was due to coronary occlusion by emboli. The source of emboli in each case was ulcerative endocarditis of either aortic or mitral valves. Myocardial infarction occured in 2 of the cases, (33) in the series of Garwin and Work.

Annesthetics--Follis(29) reports three cases of sudden death with nitrous oxide, oxygen and either in extensive arteriosclerosis of the coronary arteries.

Gallbladder and Ulcer--From a study of records of 2,737 post-mortem examinations of adult patients, it has been shown that gallbladder disease occured 2 times as often with coronary patients as with normal. There was not indication of peptic ulcer and coronary disease in the same person.(21)

## ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The coronary circulation has been the field for heated anatomical discussions. A brief description of the two arteries that surround the heart is to be found in the voluminous works of Galen and it was he who gave them their name.(13) The role of these vessels in supplying blood to the heart was first mentioned by Wm. Harvey in 1628 and Lower published the first account of anastomoses of branches of the coronary arteries.(80) Early anatomists, beginning with Ruysch in 1706, who prepared his specimens by injecting the vessels with an indestructable substance, and permitting maggots to remove the myocardium, described anastomoses.(13) The next important step in anatomical knowledge of the coronary artery was achieved by the keen observations of Raymond Vieussens. In 1706 he observed that postmortem blood clots in the heart chambers gave off small tendrils which disappeared into small openings in the walls of the chambers. This observation led him to the discovery of the first collateral channels to be described in the coronary tree. He also did much to clarify the picture of the coronary artery by pointing out and describing the individual branches of the main arterial trunks. Then Thebesius, a number of years later, demonstrated the communication between coronary veins

and the cardiac chambers, and these channels bear his name. Neither men stated whether the communicating channels were connected proximally or distally to the capillary bed.(60) The endartery theory of the coronary arteries was developed by Ruysh, Hyrtl and Cohnheim and remained till reputed by Spalteholz in 1907, who demonstrated that they are not endarteries, but have abundant anastomoses. Sine then authors have shown that an extremely rich anastomotic connection exists between the branches of the coronary arteries.(13) Another communicating channel was discovered by von Haller and consisted of branches of coronary artery which emerged from the heart and followed the great vessels to anastomose with the other arteries in the thoracic cavity. The descriptions of the intricacies and ramifications of this vascular system, clarify the pathology of practically all cardiopathies, except the acute and subacute inflammatory, and valvular lesions.

The right coronary artery arises from the right aortic sinus and emerges on thesurface of the heart between the right auricle and emerges on the surface of the heart between the right auricle andthe conus arteriosus; then, lying on the coronary sulcus, it runs to the right and downward, where it rounds the acute margin to the diaphragmatic surface of the heart. It con-

tinues in the coronary sulcus from right to left to the region of the junction of the auricles and the ventricles, where it turns to run down the interventricular groove and as the posterior descending branch, and terminates near the apex.(61) In its course it gives off small branches to the left auricles. While it occupies the auriculoventricular groove, it is sometimes referred to as the right circumflex artery. Usually as it rounds the acute margin of the heart, it gives off a large branch called the marginal artery, which in turn, gives off many large branches to the right ventricle, to the septum near the apex. The posterior descending branch also gives off many deeper branches, which plunge into the heart muscle where their arborizations end for the most part in capillaries and sinusoids.(60) The right coronary artery in the typical average heart supplies the entire right ventricle with the exception of the left third of the anterior wall. Besides this its rami ventricularis sinistri supply the right half of the heart ventricle.(63)

The left coronary artery arises from the left posterior aortic sinus and immediately after emerging divides into two main branches. The larger anterior descending branch swings around to the left of the root of the pulmonary artery as far as the anterior intervent-

ricular groove, in which it descends to the apex and usually passes, still in the groove, around the apex to the diaphragmatic surface of the left ventricle, where it breaks up and disappears in the muscle wall. In its descent, the left anterior descending branch gives off numerous large lateral branches to the left ventricle and the interventricular septum, as well as several branches to the right.

The other main branch of the left coronary artery, the circumflex, takes a course to the left, emerges from beneath the left auricular appendage, and, in the auriculoventricular groove, swings around the obtuse margin to the posterior or diaphragmatic surface of the left ventricle. While occupying the auriculoventricular groove, the circumflex branch gives off small branches to the left auricle and larger branches to the left ventricle.(61) The two main branches of the left coronary artery also gives off deeper branches which find their way into the myocardium where they arborize to supply the capillary bed and the sinusoids. Needless to say, there is frequent variation in the arteries and their branches.

Anomalies of the origin of the coronary arteries are occasionally encountered. The most common of these is the occurance of more that two openings at the us-

off at right angles into the meshes of fibrous tissue between the muscle bundles. It is thought that this arrangement permits a better circulation during systole than during diastole, or at least, as good. Anastomoses exist (1) between branches of the same artery; this is more marked in the left ventricle (2) between branches of the opposite artery, this exists in the adventitia of the aorta and the pulmonary artery, the anterior surface of the right ventricle, base of the interauricular septum, the papillary muscles and the interventricular septum. The septal wall has the best anastomosis of the heart. There are good anastomosis everywhere in the heart except in the right auricle and the auricular septum.(13)

At birth both sides of theheart are equally vascularized and anastomoses are negligible. With each decade the total vascularization is increased in the left heart, and decreased in the right. In both sides anastomosis are increased. Gross(63) states that at thirty there is "adefinite, though not yet marked, left sided vascular predominence." Jones(66) states this is present at six months, and well established at ten years. After thirty years, extensive anastomoses become evident. The heart can stand repeated insults to the coronary circulation without gross or perhaps microscopic changes in the myocardium explained on vascularity of the collateral circulation or associated circulation.(40) At forty a definite tortuosity of the arteries begins, also marked increase of subpericardial fat in which are imbeded the rami telae adiposae, the latter increase the anastomotic possibilities. During the succeeding decades, there is a progressive increase of the left vascular preponderance, of the tortuosity of the vessels, of the number of the fat vessels, and of the anastomoses of the wall and the septum, so that in the seventh decade there is relative anemia of the right side of the heart. Beck and Tichy(65) have demonstrated the importance of extracardiac circulation through the communication with ad-

jacent structures are responsible for maintanence of the cardiac circulation. The Thebesian vessels, which anastomose with each other and with the coronary veins, may under unusual conditions contribute to the intracardiac circulation.(64) From these facts the deduction can be made that a coronary occlusion in a younger individual is a more serious event than in an older one.(53)

The conduction system is supplied more or less by special branches. The sino-auricular node is supplied by branches about equally from both. The A-V node and the bundle of His receive branches about equally from both. The right limb is supplied by branches from the left coronary artery. The left by no specific branch, but by neighborhood arterioles. That right bundle branch block occurs more frequently is explained by the fact that this structure receives its blood supply from the left coronary artery which is more frequently occluded. Heart block is not common, especially in occlusion, due to the rich anastomosis in the septum around the bundle of His.(13)

Although it has been repeatedly demonstrated that anatomically the two coronary arteries communicate with each other and either artery can be injected from the other, physiologically this anastomosis must be quite limited, since occlusion of a major coronary branch

almost always results in an infarct with rapid necrosis of cardiac tissue; furthermore, the coronary system is largely isolated from the general circulation, and except for very slight and inadequate communications with vasa vasorum, the main vessel, and with circulation of the pericardium and other mediastinal structures, no important connections exist with extracardiac vascular territories. The venous system of the heart is more variable in structure than the arterial, most of the veins open into the coronary sinus, situated in the posterior part of the coronary sulcus and ends in the right atrium. A substantial but variable number of cardiac veins drain directly into the right atrium. Recently considerable attention has been directed to possible importance of Thebesian veins in the nutrition of the heart under pathological considerations. These veins are minute canals which arise in mass from the wall of the heart and open directly into the cardiac chambers. The majority open into the auricles; a few into the ventricles. 90% of the exits are in the right side of the heart.(67) It appears probably that these minute veins, normally a part of the drainage system when pressure relations are reversed, assume an irrigating function.(68) Such reversal of pressure gradients can occur when a large branch of the coronary artery is

occluded.(67) The formation of the infarct may thus be prevented by a reversal of flow of the Thebesian veins. Since only a few open into the left ventricle, little practical benefit to this chamber can be derived from that source. "It is not doubt this peculiar circumstance that makes infarction of the auricles and the right ventricle rare, and infarct of the left ventricle so common."(67)

The coronary circulation system is in part enclosed by constantly active muscle walls of the heart. Due to this circumstance the coronary vessels are subjected to constant passive variation in their caliber. This variation in caliber and aortic pressure constitute the major factor in the determination of blood flow in the coronary vessels.(67) During systole the resistance within the coronary system is obviously greatly increased. However as shown by Wiggers and his associates(69) even diring maximum systole, the intramural pressure never equals aortic pressure, and consequently intramural compression is not ordinarily sufficient to arrest coronary flow, but merely retard it. It follows that coronary flow during systole is retarded, but it is not completely arrested, because the resistance is less and because the diastolic phase is longer than systole.(40) In this end, hearts have been nourished

experimentally by coronary sinus and intraventricular perfusion and reports are found that human hearts maintained function though the coronary arteries were apparently occluded entirely or to a serious degree. (129)

Schlesinger, following injection of the coronary arteries, found that the coronary arteries are end arteries in normal and senile hearts without anastomotic connections. Anastomosis develop readily with arteriosclerotic narrowing or occlusion and are localized to the regions where needed.(130) Katz(131) also pointed out, in this end, that whenever myocardial infarction was encountered, at least two branches of the coronary artery supplying the infarcted areas were involved.

## SYMPTOMS AND DIAGNOSTIC CONSIDERATIONS

The dramatic features of sudden obstruction of a large coronary branch impress themselves indelibly upon the memory of the observer. (52) Severe substernal pain is usually the initial symptom of a typical attack. It may be located in the same areas as the pain of the anginal syndrome or may be in the upper abdomen. It is ordinarily severe, but varies considerably in intensity. Unlike the pain of angina, that of coronary thrombosis is spontaneous and does not pass off rapidly when the patient rests, but commonly persists for hours. It is not relieved by nitrites. Nausea and vomiting may accompany the pain or follow shortly after its onset. There may be symptoms of shock and collapse, especially in the severer cases. There are ashen pallor, cold sweat, clammy skin and rapid, feeble pulse which is sometimes scarcely perceptible. In spite of the intensity of the symptoms, the mind is usually clear, In rare instances, occlusion may occur without definite pain, there being possibly only a vague sense of substernal discomfort of opression. The symptoms of shock and collapse may be the only ones present, or there may be evidences of acute pulmonary congestion or of pulmonary edema. The frequent postmortem occurence of one or more small myocardial cicatrices in a patient ho gives no history of any

suggestive cardiac symptoms indicates that occlusion of a small branch may often occur as a clinically silent event. A low fever is usually seen during the first few days. There is often a moderate leukocytosis with a relative increase in the polynuclear count. The red cell sedimentation rate is usually increased. The blood pressure generally falls more or less rapidly during the first few days or hours. The fall may be moderate or marked, and the pulse pressure is usually reduced. Examination of the heart may reveal some enlargement, the anterior usually most pronounced. In spite of this, the systole is often so feeble that the apex impulse can be neither seen nor felt. The rate is generally rapid and there is frequently some arrhythmia present. When the infarction involves the upper part of the septum, heart block may be present and the rate be very slow. The heart sounds usually are quite feeble, especially the first sounds usually are quite feeble, especially the first sound of heart at the apex. This may be very faint and slapping and be entirely lacking in the normal, sustained muscular quality. Gallop rhythm is present in many cases. Localized pericarditis sometimes develops over the infarct. It is evidenced by a friction rub which may be fleeting. The presence of such a rub is of some diagnostic assistance. (12)

What we speak of as "Coronary Occlusion" consisting

of substernal pain, opression, decreased blood pressure, pallor, EKG findings, fever, leucocytosis is in reality myocardial infarction.(70,71) The attacks occur during rest (1). The collapse with decrease in blood pressure with other signs of shock are present along with congestion of systemic or pulmonic vessels which is not the case in surgical shock as brought out by Harrison. (72)

There are, however, many atypical and mild forms of acute coronary occlusion.(73,74)The initial symptom of coronary artery disease is usually either shortness of breath on exertion or sudden angina of effort or severe onset of dyspnea due to acute left ventricular failure as result of coronary thrombosis as pointed out by Blumgart. (71) He also showed that coronary thrombosis without pain is common. Davis (75) in 53 autopsy cases found only 21 gave a history of pain. Smith also pointed out that silent coronary occlusion is a clinical and pathological fact. (76) Why this should be so in certain instances is hard to explain. Most men believe with Levy (77) that heart pain is due to mayocardial anoxemia no matter how brouht on. Perhaps swallowing, chocking, gagging or dyspnea may be pain equivalent. Possibly tha nerve supply from the coronary vessels is different or these patients are hyposensative (Libman78) as

suggested by Stroud and Wagner. (79) Martin and Gorham (80) believe pain is due to coronary tension . Inadequacy of the coronary circulation, when continued, results in destruction of vessels, muscle, and nerve endings, so that a painful response is no longer experienced. Some patients complain of weakness, dizziness or sweating. In others the onset of arrhythmia, such as auricular fibrillation, flutter, heart-block or ventricular tachycardia, is only evidence there has been obstruction to the coronary bed. Dyspnea, sudden in onset and sometimes followed by other signs of congestive failure otherwise unexplained, should always arouse suspicion of coronary occlusion. (52) The further finding of a pericardial friction or EKG finding is diagnostic(53). Vague symptoms of weakness in patients with hypertension or onset of increase dyspnea with progressive failure in patients with previously mild symptoms of failure should make one alert to this condition. Any patient with a typical coronary pain with clinical findings even in the absence of posative EKG findings should be treated for coronary occlusion as clinical judgement is better than EKG. (79 ) Similarly, the occurence of acute pulmonary edema or of a paroxysm of nocturnal dyspnea, if followed by other evidences of cardiac infarction, may be due to the plugging of a coronary branch. Occasionally it is the first sign of heart disease in a person who has

is the first sign of heart disease in a person who has considered himself in good health. As a rule, the attack is sudden in onset. There may be, over a period of hours, premonitory twinges of pain relieved by nitroglycerine, followed by a more severe bout of longer duration, not yielding to nitrite medication. Blumenthol and Reisinger feel that this prodromal pain is due to intimal hemorrhage. (143) The various descriptions of coronary thrombosis pain in the literature may be summarized as follows; pain results from anoxemia of the cardiac muscle secondary to decrease in the blood supply, it is intense, unbearable and amendable only to morphing in large doses. Its location is usually under the lower sternum or in the epigastric region; the pain may be referred, among other locations to the arms and jaws. The pain is continuous and accompanied by varying degrees of shock. Steincrohn has found that pain that pain in coronary thrombosis has a characteristic rhythm or periodicity and comes and goes in cycles that is useful from the diagnostic standpoint.(144) Failure of the nitrites to afford relief is characteristic of complete obstruction of a coronary branch. The signs of acute coronary occlusion vary according to two important factors: (1) the size and location of the vessel occluded; and (2) the status of the remainder of the coronary branches with

respect to their efficiency as collateral circulation. Following a severe attack, the patient is usually prostrated, although others prefer to walk about. If a large vessel is obstructed, there are signs of shock and collapse. The pain is commonly present for at least an hour and may last for the better part of a day. The heart rate is rapid and the blood pressure falls. It may be as low as 50 or 60 mm. of Hg. In the hypertensive patient, the fall is not as great as in one with normal blood pressure prior to the acute episode. Weiss (87) shows an early rise in the pressure in coronary thrombosis with a later drop in both systole and diastole. This is the best means of differentiation from angina where the pressure increases. The heart sounds are weak and tic-tac rhythm or a gallop may be heard. The heart, as in result of sudden impairment, frequently dilates. If the myocardial function is seriously impaired, heart failure with pulmonary congestion and a rise of venous pressure follows. In closure of a branch of the right coronary artery there may be acute, rapid swelling of the liver (Libman). Transient glycosuria is sometimes an effect of disturbance of the autonomic nervous system (78) and in a patient seen for the first time, arouses what may be falsely suspicioned of the existance of diabetes mellitus. (3 ) The low blood pressure and slowed circulation

may lead to suppression of urinary secretion. Occasionally, jaundice appears. In some cases, the heart ceases to beat within a few minutes.

With the formation of an area of infarction involving the pericardial surface, pericarditis develops and a friction rub may be heard. (82) This may appear within the first few hours and is often evanescent; sometimes lasts for days, being audible at time and not at others. Harrison finds it occurs between the second and the seventh days lasting only a few hours (72). If the infarct is on the posterior aspect of the heart, the rub is not audible. The detection of a pericardial rub leads support to the diagnosis; its absence does not exclude it. The temperature generally rises. There is always a latent period, ranging from 6 to 12 hours between the development of the infarct and the appearance of fever, coinciding with the time necessary for necrosis of the cardiac muscle. The temperature, ordinarily reaches a level of 101, may go to 102 degrees F. or higher by rectum while at the oral region it may be normal due to the shock present. The height of fever and its duration vary according to the size of the infarct and depending upon whether the subsequent course is uneventful. As a rule the fever subsides in a week with prolongation of the pyrexia indicating a complication. The leucocyte

count is characteristically elevated and may rise within a few hours after onset. (83) It commonly ranges from 12,000 to 20,000 white cells per cmm., but may go to 33,000 in an uncomplicated case; remaining elevated for a week or more. The percentage of polys is increased; and in cases with only slight leucocytosis, this relative increase may be of considerable diagnostic aid.(52) The increase after the first two or three days of illness, is of importance indicating the presence of some complicating factor. (84) It may be due to extension of the thrombus or an increase in the size of cardiac infarction, or form extension of a mural clot within the cavity of the heart. If the coronary accident has occurred without pain, hemoptysis, due to pulmonary embolism, may be one of the first signs which, by proper reasoning, leads to the correct diagnosis. (85) The sedimentation rate of the red blood cells is modified by the formation of a cardiac infarct. (86) It is increased, usually on the second or third day, to a level of between 50 and 100 mm. at the end of an hour, and remains elevated, as a rule, for a considerable time after the subsidence of fever and leucocytosis. It is frequently higher than normal for a period of several weeks, and there is some evidence that this test is a good measure of the rate of healing of the area of myocardial softening. Complications serve to maintain an

elevation in rate or to raise it still further. This test would prove to be a helpful aid in judging when a firm scar has formed and, hence, in deciding upon the proper time for permitting the patient to get out of bed. Physical findings are of no particular significance except for the general appearance. A picture of agitation and shock withevidence of extreme pain and aprehension is presented. On examination of the heart, the beat is weak with no visable or palpable apex impulse. In quality, the heart sounds are muffled or distant and especially in the first sound at the apex. The rhythm may be of gallop with pulsus alternans and pericardial friction rub common. In the abdomen the liver may be enlarged and abdomen rigid, often an icteric tint is present due to hepatic engorgement; also rales of lungs may be present in their bases.

The picture as pictured so far may be regarded as the common pattern. There is no rigid adherence to this type. With occlusion of a small branch and the formation of an infarct of corresponding size, the signs are less marked. The fall in blood pressure may be inconspicuous or may be delayed for a day. The leucocyte count rises but little and fever, if present, is slight and transitory. There is a group of ambulatory patients with a history of substernal or precordial pain of some

hours duration. It may be sharp at first or there may be only a persistent dull ache. It then subsides and they feel perhaps not quite up to par after the attack. They may have subsequent twinges. Frequently they do not know whether fever was present. The EKG may show slight deviations from the normal on the first examination: of greater importance are successive records which, if taken at intervals of a day or two, often exhibit characteristic alterations. Such mild cases are not uncommon. It is important that a correct diagnosis be made, in order that, following such an episode, proper measures may be taken to safeguard the heart from further damage. Otherwise occasionally, their sudden death a few days or weeks later, afford proof of the correctness of the diagnosis. It is hard to make only in the atypical case.(52)

DIFFERENTIAL DIAGNOSIS AND EKG FINDINGS

The most difficult differentiation is angina from coronary thrombosis. ( 1 ). The most important difference is the duration and severity of pain: in angina it lasts for minutes while in Coronary thrombosis it lasts for hours and days. This differentiation is important on account of the markedly different type of management. Oille reports the operative mortality is six times as great in thrombosis as in angina. In angina EKG change

in angina are temporary; in occlusion they are permanent and progressive.

| | Angina Pectoris | Coronary Thrombosis |
|---|---|---|
| Pain: | | |
| 1. Intensity | Less severe | Usually severe |
| 2. Duration | Minutes | Hours or days |
| 3. Character | Tightness | Same but more marked |
| 4. Extent | more limited | More widespread |
| 5. Location | Substernal & Rad. | Same |
| Attitude: | Stands still | Restless (not in bed) |
| shock | Slight | Frequently marked |
| Onset | With exertion | At rest, after meals |
| | | Early A.M. |
| Dyspnea | None | Frequent |
| Pulse rate | Not changed | Increased |
| Blood press. | Frequently increased or normal | Decreased |
| Heart sounds | Unchanged | Frequently changed |
| Vomiting | None | Frequent |
| Fever | Absent | Present |
| Leucocytosis | Absent | Present |
| Sed Rate | Normal | Increased |
| Circulatory fail. | Absent | Frequently follows |
| EKG | Changed in paroxysm | (Charasteristic) |
| Enlargement | Absent | Present; atonic type |

Severe attacks of coronary thrombosis may simulate an acute surgical abdomen with symptoms suggesting a perforated peptic ulcer, biliary colic, acute pancreatitis, bowel obstruction, or even acute appendicitis. The following signs and symptoms may be present: (1) Pain confined to upper abdomen. (2) Vomiting not rare. (3) Jaundice, at times, after several days; usually due to autolyzing pulmonary infarcts. (4) Marked rigidity and tenderness of epigastrium and right upper quadrant. (5) Fever and Leucocytosis.

Differentiation may be possible by the following:

(1) Muffled heart sounds, gallop rhythm, alternating pulse
(2) Previous history of "Indigestion" on exertion
(3) Tightness of chest
(4) Radiation of pain not typical for abdominal disease
(5) More apt to have dyspnea with coronary dis.
(6) Pain: Rarely epigastric alone, but also substernal
(7) Age: Victims of coronary thrombosis elderly men predominating.
(8) EKG fairly typical

Pulmonary embolism, when lodged in the lower right lobe anteriorly, presents the same problem.(13)

Oille(87) said,"The mistakes made now are in the reverse of those made 10 to15 years ago. The coronary thrombosis was not diagnosed when it should have and now it is made when the pain is obviously due to gall-bladder colic or other abdominal organs." Early symptoms of the heart disease may be similar to indigestion relieved by belching or soda. Butch, McGowan, and Walters(88,89,90) have shown nitroglycerine will relieve the pain of gall-stone colic, this complicates things further. If in doubt of the heart take an EKG. Connell says the best differential points are dyspnea, which occurs only rarely in abdomenal cases and also auricular fibrillation, flutter and ventricular tachycardia. He also suggests the frequency of gall bladder attacks with coronary disease and visa versa occurs too often to be a coincidence. (91)

Sudden pain over the lower sternum or epigastrium with nausea, vomiting, tympany, feeble pulse, ashy color,

cold sweat with collapse all suggest gall bladder disease, acute pancreatitis, perforated ulcer, hemorrhage into adrenal cap; while dyspnea, hyperresonance of the thorax with obscured heart tones suggest pneumothorax or diaphragmatic hernia, both being excluded by emphysema changes bilaterally, persistant breath sounds, rales, and failure of the heart to be dislocated. ( 5 ) Pneumonia may be ruled out by chest pain unrelated to respiration, no pleural pain, temperature is too low and no sputum in coronary thrombosis. Also a previous history of angina will give one a clue to diagnosis.

Acute Cor. Pulmonae due to pulmonary emboli causes severe sudden pain with circulatory collapse, EKG findings are similiar in both and both can occur following operations on the extremity and pelvis. This is hard to diagnose is patient dies early.(92)

In cases of hemiplegia not due to hemorrhage, coronary thrombosis should be considered. ( 1 )

Nephritis, the urine in coronary thrombosis can be similiar to active nephritis with albumen, casts and cells with occasional hematuria. The urine returns to normal when recovery occurs. The urine also shows glycosuria with shock making a picture similiar to diabetic coma at times.

Coronary insuffiency is so common that differential

is important from coronary occlusion. EkG findings may be distinctly different in the two conditions (93 ). The depression of the RS-T segment and changes in the Q wave in coronary insuffiency with elevation of RS-T segment in coronary occlusion, particularly in lead I. The presence of depressed RS-T segment in coronary insuffiency is due to subendothelial localization of the infarct (94). Another differential test for coronary insuffiency is suggested by several who found the anoxemia test is good index of the coronary reserve. A posative test means coronary insuffiency while a negative result doesnt exclude coronary disease. This is an aid in differential between coronary insuffiency and other disorders.(94,96) This was confirmed by Levy, Bruenn and Russel in the use of EKG changes caused by induced anoxemia test for coronary insuffiency. ( 95 )

In spontaneous Pneumothorax, the symptoms may at times be the same as with coronary thrombosis. The diagnosis is made by EKG and radiographic assistance. This is not always good since by rotation of the cardiac axis the Ekg findings may be the same as coronary thrombosis with T wave anomalies, ST deviation and absent or reduced posative initial deflexion in the standard lead IV. (97 )

Premonitory pain--recognition is important from the diagnostic and therapeutic standpoint. They result from

pure arteriosclerotic processes whose origin and progress are unrelated to physical activity and rest; are not associated with myocardial infarction, no fever, leucocytosis, tachycardia or decreased blood pressure. All are significant in the differential diagnosis. (98 )

EKG FINDINGS

Although recognition of cases of coronary thrombosis at the bedside or clinical diagnosis before the use of the EKG was generally made, the latter added materially to criteria we use in diagnosis,( 1 ) It is used to advantage in acute stages and to some degree in detection of previous attacks. Wearn (83 ) called attention to low amplitude of the EKG in 2 of his patients, this is valuable but not pathonomonic. The most important change was noted by Pardee( 99 ) who noted the formation of the complexion between the downstroke of the R wave and end of the T wave changes. This is disappearance of the interval between the initial venticular deflexion and the terminal ventricular deflexion T. Also the T wave begins in the downstroke of the R wave before it has reached the base line. The low takeoff of the T wave from the upstroke of the S wave before it has reached the base line is common. When such changes are marked in the R-T interval they are practically pathonomonic of coronary thrombosis. This is also seen in acute

rheumatic fever. (100 ) but is not so marked, also in uremia and pneumonia but the T waves are not in the peculiar rounded hump of coronary thrombosis. These EKG changes may occur in a few hours after the onset (101 ) as seen by Rothschild, mann, and Oppenheimer or may not develop till later. Their absence doesnt rule out coronary thrombosis. These changes change from day to day as seen in no other condition but coronary thrombosis. A final EKG feature is the presence of a prominent Q wave in lead III. Its significance is unknown. ( 1 ) Riseman, Waller and Brown found changes in EKG were constantly depression of the ST segment and T wave changes with diphasic T waves in 1 or more leads. ST and T changes most stricking in the precordial lead and changes following induced anoxemia were similiar except for heart rate. ( 102 ) The presence of a Q2 in addition to prominent Q3 lends further support to presumptive diagnosis of coronary disease as shown by Boyler.( 103 ) Bohning and Katz feel that low voltage in 3 leads in anterior infarction with lead IV normal is common. Lead IV is a definite aid in diagnosis of a recent infarct due to coronary occlusion especially anterior.(105 ) Alteration in the T wave doesnt mean myocardial infarct or dammage but melely indicates a response of the heart to anoxemia. (May104 )

The proper differential diagnosis between Ventricular tachycardia and auricular tachycardia or flutter with proper treatment, is important since it may make the difference between life and death of the patient. ( 106 ) If the EKG is available the diagnosis is not difficult, but in as much as most patients are in homes when suffering from coronary disease, bedside aids in diagnosis are of primary importance. Four instances enable us to make the proper beside diagnosis:

(1) In auricular fibrillation the rhythm is absolutely irregular; here it is regular except for a slight irregularity heard over the precordium. (107)
(2) Uninfluenced by vagal pressure (vent. Tachycard.)
(3) Intensity of 1st sounds of heart at the apex vary in ventricular tachycardia.
(4) The rhythm although regular, will now and then be interrupted by a slight pause readily detect- by the ear. ( 108 )

In general the EKG usually gives valuable evidence in coronary artery disease. In angina these changes are temporary; in occlusion they are permanent and progressive. These changes are apparent in the RST interval as an elevation, depression or rounding. These changes are usually followed by the inversion of the T wave. Wiggers (13) ( 109 ) explains the changes in that infarcted areas lose their power of contraction and conduction. The action potentials are modified and the contour of the EKG is affected. This has been produced experimentally by producing necrosis of the ventricular wall or ligating the

left coronary artery. ( 13 ) A diagnosis can be made from clinical evidences alone in a majority of patients. The EKG frequently reveals changes which are of great help in diagnosis and in doubtful cases it may be the determining factor. Consecutive records are more valuble than single ones and the use use of precordial leads may be essential. The alterations in the EKG are scarcely pathonomonic and they should, therefore, always be considered in relation to other evidences as revealed by history, symptoms and physical examination. ( 12 )

Localization of the infarct

When the infarcted area involves the anterior and apical portions of the heart, including the left lateral wall. it is likely to produce changes in the EKG of the Q1T2 pattern. Lead I shows low potential of QRS and lar- Q wave. There may be a Q wave in lead II and there are uaually large S waves in leads II and III. In revent infarction, the R-T junction and segment are displaced upward from the isoelectric level, and as healing begins the junction and segment return to normal and the T wave in lead I becomes sharp V shaped inverted wave. The precordial lead which corresponds to the Q1T1 pattern usually shows a large negative initial deflection or Q wave and the R-T junction segment and the T waves are progressively altered exactly as described for lead I.

Such infarctions are commonly located in the course of the anterior descending branch of the left coronary artery. Infarction of the posterior and diaphragmatic walls yields the Q3T3 pattern. There is a large Q wave in lead III, often also present in lead II. QRS is of low amplitude in lead II. In recent cases there is elevation of the R-T junction and segment in lead III. This is followed during healing by their return the isoelectric level and by progressive change in T3 which becomes V shaped and negative. T2 may follow T3. The precordial lead is less consistently altered and may remain normal. When altered there is likely to be a negative displacement of the R-T junction and segments present in the acute stages. Mixed types of these alterations are not infrequent. Other significant changes in the EKG include splintering and prolongation and the QRS complexes as well as such arrhythmias and A V block, auricular flutter and fibrillation and auricular tachycardia. ( 12 )

## PATHOLOGICAL CONSIDERATIONS AND COMPLICATIONS

In the consideration of infarction of the heart from the point of view of morbid anatomy, the relationship of coronary disease to the infarction has long been understood. Weigert in 1880 showed that infarction of the heart was analogous to infarction in other organs. Ziegler introduced myomalacia cordis as a term referring to infarction of the heart. In 1881, Cohnheim and von Schultess-Rechberg studied the pathologic anatomy of experimental coronary infarction in dogs and emphasized the conception of the coronary artery as an end artery. In 1907, Hirsh and Spalteholtz showed that coronary arteries anastomose with each other. Gross and Wearn and others demonstrated the remarkable anatomical features of circulation in the heart. The experimental study of coronary infarction has been continued in recent years by Smith, Miller and Matthews, Karsner and Dewyer, publishing splendid studies of the gross and microscopic pathologic changes in experimental infarction in its various stages. The correlation of the pathologic findings with the sequence of events enables us to anticipate not only the possible variations in the clinical picture, but the probable time relationship of such changes, leading to a more intelligent prognosis and rational therapy. ( 1 )

The pathological picture of coronary thrombosis is variable, depending on the size of the occluded vessel and the rate of occlusion. If the smaller vessels are occluded, acute episodes do not occur, and the resultant condition is dubbed "chronic myocarditis." An infarct is usually smaller than the vascular field of the occluded vessel, depending on the abundance of the anastomoses which are capable of supplying its periphery. This would usually be more favorable in later decades as shown by Gross. ( 63 ) However, previous insults, especially to smaller vessels resulting in scars, might offset the advantage gained by age. The vascularization of the infarct largely determines the final outcome. Factors, which determine this are: (1) the collateral stream bed must furnish the same amount of blood as the occluded vessel; (2) the more circuitous the collateral vessels the larger their channels; (3) anastomotic branches given off at acute angles deliver more blood; (4) the condition of the vessel walls of the vascular bed (elastic walls enlarge easier): (5) good strength of heart beat is necessary to open new channels. If a vessel gradually narrows before it becomes occluded, the anatomotic bed is enlarged and prepared for it. Vascularization is then more complete and rapid.( 13 )

The most frequent site of occlusion has been con-

sidered in the anterior descending branch of the left coronary. In fact, it has been called the "artery of sudden death." The recent work of Barnes and Ball(119 ) does not corrobrate this. In forty-eight cases of coronary thrombosis they found twenty-eight occlusions of the left coronary artery and twenty on the right. They divided occlusion into three types:

1. Anterior apical type, due to occlusion of the anterior descending branch of left coronary, involving the apex and the anterior portion of the left ventricle and the adjacent interventricular septum.

2. Mid ventricular type, due to occlusion of the circumblex branch of the left coronary artery, involving the obtuse margin of the left ventricle about midway between the base and the apex.

3. Posterior basal type, due to the occlusion of a branch or the main trunk of the right coronary artery, involving the posterior basal portion and the adjacent interventricular septum and rarely the small border of the adjacent right ventricle. (13 )

In coronary artery disease, the underlying mechanism of myocardial infarction is a relative disproportion between the requirements of the heart for blood and the supply through the coronaries. ( 71 ) Changes in the coronary arteries are the only constant feature. (111) In careful search of the coronary arteries at autopsy, no significant changes may be revealed to adequately explain the sudden death which so commonly occurs even with the first attack of coronary symptoms.(52,1) Death may occur so rapidly that there is not sufficient time

for any detectable change to be produced in the heart muscle. ( 52) In two cases of complete occlusion of both coronaries at their orfices, the myocardium was unaltered; the heart having been adequately supplied by Thebesian veins.(116) R. Marie and Benson ( 67 ) have called attention to the fact that infarct formation may be overlooked in the gross specimens, where only microscopic changes exist. Allen (112) found only 371 gross lesions in 1000 cases of consecutive autopsies. Of these, 238 showed pathological patch or diffuse fibrosis, 178 showed fibrosis with fatty change and 48 with fatty change alone. Sutton and Brandes (113) found in 340 autopsies with gross lesions of the coronaries, definite macroscopic scars in only 81; 46 cases examined microscopically showed sclerosis of the smaller vessels and microscopic scars in 43 cases. More often, a variable degree of atherosclerosis of the vessel walls may be recognized. The picture under these circumstances is one of atherosclerosis with plaques of varying size and thickness, at times almost shutting off the lumen of the vessels.( 1 )

Bedford ( 117) in 1939 pointed out the fact that the clinical term, Coronary Thrombosis, is commonly employed to include cases in which an infarct of the heart is believed to be present although no thrombosis of the art-

ery may at times be demonstrated; only an atheromatous stricture of the artery. By Lowe's differentiation, an atheroma is the deposition of cholesterol material in the deeper layers of the intima of the artery. Early it is reversable but later it is associated with proliferative intimal production of a plaque which encroaches on the lumen of the vessel with atrophy of the media ultimately. This process is most serious in the smaller vessels; while arteriosclerosis is essentially change of the media. Hypertrophy of the elastic and muscular layers with late degeneration and fibrotic change so that vessels inrease in length and become tortuous.(118)

In the typical case, this underlying atherosclerotic process is accompanied by the production of a thrombus which may or may not occlude completely the coronary artery involved. The coronary arteries are not strictly end-arteries but their anastomosis are usually inadequate to assume function of a large branch as the descending rami. ( 12) The point of occlusion is usually found in the anterior descending branch of the left artery, but may occur anywhere in either vessel. Barns and Ball( 119 ) found in 48 cases of coronary thrombosis that 28 were in the left, and 20 in the right coronary artery. Less often the occlusion may occur from other causes such as bacterial emboli from an endocarditis,

syphilitic involvement of the aorta and ostia of the coronaries, but far the most important and most frequently encountered cause or coronary occlusion is the simple arteriosclerotic process either alone or complicated by secondary thrombosis. ( 1 ) Occlusion occurs in three ways: (1) hemorrhage into the intima of an arteriosclerotic plaque with secondary thrombosis in the lumen due to injury or disolution of the overlying endothelium. (2) primary thrombosis of an arteriosclerotic plaque. (3) rarely hemorrhage into atheromal abscess, hematoma occluding the vessel mechanically without thrombosis. (120) The immediate cause is liberation of a thromboplastic substance from the lesion in the walls of the artery, particularly those affected by advanced arteriosclerosis. Increased intracapillary pressure due to persisting hypertension is the major factor in formation of intimal hemmorrhage and the precipitation of coronary thrombosis. (14)

The effect on the myocardium deriving its blood supply from the diseased vessel, varies from gradual degenerative changes in the mild case to frank coagulation necrosis as seen in the typical infarct in severe cases and spoken of as myomalacia cordis. In the mild case, obstruction to the coronary circulation results in a localized anemia of the heart muscle and is

accompanied by all the degenerative changes associated with such anoxemia. Fatty degeneration is perhaps the most outstanding of these phenomena, but in many instances it is difficult to detect it without use of osmic acid or frozen sections with use of fat solvent dyes. There is a universal tendency for this to follow a symmetrical pattern with alternating areas of relatively uninvolved muscle fibers giving rise in marked cases to the characteristic gross tigroid mottling. Accompanying this fatty degeneration, not infrequently, hydropic changes and granular changes of the cytoplasm are also demonstrable. One of the most striking lesions as seen in the heart muscle is the so-called fragmentation of the muscle fibers, representing a fracture of the muscle fibers at the intercalary disks.(1) A prominent adventitial perivascular infiltration of lymphocytes was often encountered in arteriosclerotic vessels as found by Horn and Finkelstein (15).

The changes in the myocardium depend solely on the extent and duration of the relative ischemia and not on the manner produced.(71) In myocardial infarction due to coronary insuffiency there is no acute obstruction but merely impairment of the coronary circulation resulting in necrosis of the heart muscle as caused by strain, effort in the face of coronary artery disease.

(34)

In the severe case, when the occlusion becomes complete through the combined atherosclerotic and thrombotic processes, then infarction follows. ( 1 )

Ziegler's classical description of infarction in 1887 is as follows:

"the appearance of the softened areas varried according to their age and blood content. Shortly after the beginning of the anemia they are firm and manifest themselves only by a dull yellow coloration of the heart muscle. After some time they become soft and friable and maintain a yellowish-white coloring; sometimes the cut surface sinks in somewhat as the tissue is already softened. If the obliteration and occlusion of the arteries are followed by the escape of blood from the capilaries; ie, by hemorrhagic infarct formation, then the areas are from the beginning either dark red with brown and yellow patches, or red in the periphery andyellow in the center. After some time they become grayish-yellow or brown, or perhaps of a rusty color. Both anemic areas later acquire a gray transparent appearance, and retract somewhat below the level of the surface made by sectioning. The areas of softening occur mostly in the apical portion of the front or back wall, sometimes in right ventricle or rarely in the auricles, and occassionally in the papillary muscles where the whole papillary muscle may be converted into a brittle yellow area in hemorrhagic infiltrated tissues. If this softening extends to the intima, thrombi develop to form heart polyps, or if it is extensive and reaches thru the whole muscularis, rupture of the heart wall occurs.

The tissue changes are partially regressive, partly progressive. The anemia produces destruction of numerous muscle cells, and accordingly in the yellow appears areas are muscle fibers in various stages of disintegration, clouding or homogenous degeneration occurs, withfragmention, and finally the transition to granular detritus. In small areas of softening the process may end with the destruction of the muscle cells, but in other cases the connective tissue also suffers changes, where the nuclei in places no longer stain and granules are deposited in the pale fibrils. In cases of hemorrhage, red corpuscles in their normal state or in various stages of disintegration may be present, or only pigment granules may remain. In rupture of the heart

wall the site of the rupture is infiltrated with blood. When a certain stage is reached the reparatory process starts: round cells wander out of the vessels, and a reactive inflammation occurs; the detritus is phagocytized or disolved and absorbed, and granulation tissue and connective tissue forms. Thus the necrotic area becomes replaced by scar tissue. These scars may be reddish gray or transparent gray, but become firm and white as they lose their cellular elements. If the scarred area is extensive the pressure of the blood may produce an outpouching of the wall as an aneurysm." (53)

If this process is very extensive, involving any of the major branches of the coronary and causing complete degenerative changes to occur, a picture of softening follows which is spoken of as myomalacia cordis. This may perhaps best be described as the point at which the maximum tissue changes occur. At this point the muscle shows coagulation necrosis. The cytoplasm loses its striations and tends to stain homogenously and rather more intensely with eosin. The nuclei may not be seen or show marked degenerative pyknotic and karyorrhetic changes. The area of infarction is extremely irregular as compared to organs with end-arteries as spleen and kidneys. In other areas, particularly near the edge, degenerative processes are paramount. The cells are swollen and show fatty, granular and hydropic changes. Interstitial edema of the supportive stroma occurs and a variable amount of cellular infiltration follows. Accompanying this degenerative softening of the wall of the heart, there follows obviously intimal damage

with the development of a mural thrombus at the site of the involved area. This is in the nature of a protective mechanism and may at times aid in the reparative phenomena through its organization and with a resultant thickening of the endocardium. ( 1 ) Stewart and Turner noted pericardial involvement in 88% of the cases of coronary thrombosis with myocardial involvement in a series of 275 cases.(121) Gradually the musculature undergoes lysis and the phenomena or repair sets in. The end result in such a case is replacement fibrosis which ultimately contracts down to typical scar tissue. Involving as it does most frequently the left descending branch, the apex of the left ventricle is the most frequent site of such extensive infarction. In healing ther is often left merely a thin fibrous wall instead of the usual thick musculature. This at times may bulge to form an aneurysm. In milder forms of such circularoty distrubances, a moderate degree of anemia to the part follows. (114) This may result in the actual destruction of a certain number of muscle fibers which are replaced by fibrous tissues in replacement type of fibrosis called myosclerosis. (114)

Tigerstedt (122) states that the coronary circulation claims ten per cent of the total ventricular output. Practically all cases of so-called chronic myo-

carditis(degenerative heart disease, Christian's non valvular heart disease) are due to coronary vascular thrombosis. They are also referred to as indurated, fibrotic or fibroid hearts. (13)

Complications

These may develop at any time. Mural thrombosis may occur over the infarct within the ventricle and give rise to embolism in various organs of the body, (123) pulmonary and cerebral infarctions (125,53) be- the commonest. Aneurysm and rupture of the coronary arteries has been rarely observed; Packard and Wechsler who credit Bougon(1812) with reporting the 1st case, found 29 cases in the literature to which they added one. Etiologically they were of a mycotic, embolic and arteriosclerotic origin.( 128) Benson( 127) quotes Vestberg who collected 59 cases and added one of his own of dissecting aneurysm. He classifies them as parietal, septal, valvular and inter-parietal; the point of predilection being the junction of the heart and aorta. Rupture of the ventricle with prompt death occurs occasionally, most frequently toward the end of the first week when softening of the infarction is the greatest. Leonard and Daniels (124) report 21 cases of perforated interventricular septum due to coronary occlusion where the lesion was varified and 4 where the diag-

nosis was made antemortemly. Rupture occurs most frequently at the apex because the ramus descendes anterior sinster is the most common site; rarely at the base. (124, 53) Although premature ventricular beats and some degree of heart block might properly be included as complications. Involvement of the conductive systems in its main branches give rise to partial or complete block. ( 118 ) They are so often present that usually they are considered to be part of the clinical picture. Sutton( 53 ) mentions pericarditis with pericardial adhesions rarely with effusion into the pericardium. If the infarction extends to the visceral pericardium there occurs a non-infectious pericarditis. Paroxysmal auricular fibrillation is a complication of rather frequent occurence. Injury to the muscle may alter its irritability locally and give rise to extopic beats, extra-systoles, fibrillation and also auricular involvement if the auricle is involved. (118) The paroxysm may last for only a few beats now and then ard are then readily overlooked, or they may persist for much longer periods of the time and are recognized with ease. Their appearance does not seem to influence the patients outlook. Paroxysms of ventricular tachycardia, while much less common, may be of serious import. Although it is occasionally possible to identify such

paroxysms by the usual methods of clinical observation, this can seldom be done with accuracy except by an expert. Their presence, however is to be suspected if the heart rate jumps to a level above 160 and the rhythm remains essentially regular. Ventricular fibrillation may follow ventricular tachycardia, or may occur independently. It generally causes almost immediate death. The condition is readily recignized in the EKG. (12) Askey mentions persistant painful disability which restricts movement of the shoulder and causes swollen fingers; the sequella of myocardial ischemia causing cardiac pain, in the shoulder, pain, and hand pain all due to myocardial ischemia and pre-existing arthritic lesions of the shoulder and hand.(126) In cases where the patient doesnt die in a few days, the patient may live for weeks or more in various degrees of decompensation. Not infrequently a history can be obtained with cardiac failure due to cardiac infarction. This complication of gradual myocardial failure is a common early event originating with a cardiac infarction, however, at autopsy fibrous scars of an ancient infarct are frequently found in patients in whom no history pointing to coronary thrombosis had been obtained.( 53 )

## COURSE, PROGNOSIS AND THERAPEUTIC CONSIDERATION

Death may be almost instanteous or may be within a few minutes. These cases have often been diagnosed erroneously as instances of death from "Acute indigestion" owing to the presence of epigastric pain and of vomiting. Such cases are the exception and the seizure may persist with partial amelioration for a few days, then be terminated by death. When the patient lives for more than four or five days to a week, recovery is likely to ensue. This recovery may be so incomplete that the patient remains bedridden and within a few weeks, or months develops a progressive heart failure from which he dies. In other cases, recovery is sufficient to allow the patient to lead a greatly restricted life for a few years. Finally, healing may be complete and the patient may become about as well as he was prior to the occlusion. Such cases are usually those of closure of the medium-sized branches of the artery. Subsequent attacks are frequent. It is to be borne in mind, that however favorable the progress may seem to be, the patient remains in serious danger until at least three weeks have elapsed since the onset. At any time during this period the heart may rupture or a fatal attack of ventricular tachycardia or fibrillation may develop. Less than 30% of the first attacks

are fatal.(12)

Prognosis is much more favorable than has been assumed. Heberden states that "often angina pectoris continues many years with out any injury to health apart from liability to pain on exertion." Today, with differentiation between angina pectoris and coronary thrombosis usually possible, this is still mor true. In regard to coronary thrombosis, Parkinson(133) recently states, "When a patient has weathered for a few days even an intense attack, the natural expectation should be that he will recover with a fair degree of health, even good, which may continue for years. A second attack is relatively infrequent." White recently reported two cases: one had an attack of coronary thrombosis at 63, passed insurance examination at 65, climbed mountains at 72, and died at 80 of apoplexy. Another case, age 67, having had three attacks, is living and active but with some substernal distress twenty years after the first attack. He has also published a larger series of cases in which the average duration of life after a coronary occlusion was 2.4 years and 4.9 years, after the onset of angina pectoris.

During the first few days of an attack of coronary thrombosis the prognosis is difficult, Levine states, "No single feature seemed relisble as an indicat-

ion of a good or bad prognosis. Mild cases occasionally died and very severe ones recovered." For reasons mentioned, the older age groups should have a better chance of recovery. The degree of shock, dyspnea, fall of blood pressure, degree and duration of pain, fever, leucocytosis, extent of cardiac dilation, changes in rhythm, particularly ventricular fibrillation, all have some bearing on the outcome.(13) Prognosis is best in the young, while severe heart failure is an ominous sign, as is a blood pressure below 90 systolic or if the patient is stuporous or unconcious. (72 ). The criteria for prognosis in individual cases is most unsatisfactory. In general about 50% have immediate recovery. No single feature seems to be reliable as indicative of a good or poor prognosis. Apparently mild cases died and severe ones recovered. Slight differences in mortality were noted when certain factors were analyzed such as age, sex, development of pericarditis, and auricular fibrillation. Ventricular tachycardia and heart block seemed to have a greater mortality than the average. Even the type of change in the EKG had no influence on whether the patient would recover or not.(3)

The variability in the time death occurs and the mechanism of fatal events may be divided into groups:

1. Immediate death probably due to ventricular fibrillation or cardiac standstill.
2. Circulatory failure(1 to several hours) with shock, blood pressure 60 to 80 mm. with no perceptable pulse.
3. Cerebral embolism--usually in the second week, none noticed after the 6 week.
4. Congestive circulatory failure occuring 1 to 3 mo.

Recovery occurs in three types generally:

1. Previous angina, These improve following attacks, with blood pressure falling and staying low following attack. These patients become ambulatory with no further angina. It follows that drop in blood pressure is a welcome sign if it doesnt raise as recovery takes place.
2. Angina returns after attack whether they had it before or not. The fall in blood pressure didnt occur and rose after the attack. Here angina limits the activity to some extent. This is the next most favorable type of recovery.
3. Lastly those that develop greater or lesser evidence of general circulatory insuffiency as the days and weeks progress, dyspnes, edema, enlargement of the liver, hydrothorax develop which may or may not respond to therapy. Persistant auricular fibrillation may be found here. Early circulatory failure symptoms may be temperary but if present weeks after the attack, this is an ominous sign.

Recovery following cerebral embolism leaves one withhemoplegia or the like. Other cases show both coronary failure and angina or may develop angina or coronary failure later or may have other attacks of coronary thrombosis. Not withstanding these abberations the general division into the above three groups will be applicable in most cases.(1)

Immediately the general mortality is approximately 53%. After recovery in 143 cases the average duration was 24 months including 42 still living. Of those who

eral the more severe the initial symptoms, the greater likelihood of permanent impairment, but this is not invariable. Subsequent attacks add to the gravity of the outlook but as many as 6 consecutive infarcts have been reported in the same person with recovery following.(44) To adopt an attitude of optomism is not only good practice but justified by facts of experience.(52)

If the individual with coronary disease pain has a negative ekg, examination of the heart and physical findings, the prognosis is good.(40)

Both Williams(148) and Feil(149) suggested that gradually forming thrombosis in a stenosed coronary artery is out most probable cause of premonitory pain. If this be so the development of such pain assumes important diagnostic and prognostic significance. Sampson and Eliaser(150) discuss possible importance of enforcing bed rest immediately with the appearance of premonitory pain. It is now generally appreciated that a more cheerful attitude regarding the prognosis of coronary thrombosis is justified.(151 152) Immediate mortality for the first 6 weeks is less than 20 to 25%. In general favorable prognosis is indicated by youthfulness, absence of history of previous attacks and typical ekg changes might occur in multiple infarction or antecedent myocardial damage therefore giving unfavorable prognosis.

Very low amplitude in all leads is a poor sign. The impression that posterior infarction has better prognosis than the anterior is called into question.(152) (153)

Therapeutic considerations

The treatment of a coronary thrombosis is divided into that of (1) onset or acute stage, (2) the healing phase, (3) the convalescent, and (4) the permanent management (reestablishment of patient with disability)(13)

Except in syphilitic origin, the treatment is largely symptomatic. In the acute stages, the two most important measures are rest and morphing. The latter is especially valuble to lessen pain and restlessness and to diminish pulmonary edema and cardiac asthma by influence in the function of the left ventricle. Often as much as 1 grain in a divided dose is necessary in a few hours.(52) As is so well known it is absolutely essential . d cannot be replaced by any other drug. For persist pain, the oxygen tent(50%) not only relieves pain b t prevents tissue necrosis.(136) Brown has recently repor ed the relief of the pain at the onset from intraven of euphyllin. Recently Levine, Prodgert (135) advised against the discriminate use of as they believe that the vasodilating effect may ncrease the area of thrombosis, or even cause it. and Smith, however(137)

demonstrated that the nitrites difinitely increase the coronary flow. This effect being more evident than the lowering of the blood pressure. The logical deduction seems to be, that with shock or low blood pressure, they are contraindicated.

Medical Treatment

The acute stage is chiefly characterized by the paucity of medication, and such as is used, to meet only definite indications. A competent circulation at low ebb is to be desired. Stimulants are to be avoided as they may cause ventricular rupture or dislodge an embolism. It is, however, safer to use them during the first twelve hours than later.(13)

Rest--Six to eight weeks in bed is the minimum requirement for adequate healing as indicated by normal temperature, leucocyte count, sedimentation rate in absence of pain and myocardial insuffiency. Here gradual resumption of activity follows.(52)

Diet--Restriction is advocated by Master, Jaffe and Dack (152) (155). Small quantities of milk, orange juice, and glucose are allowed the first week; then, if improvement follows the diet is increased to 800 calories each day, and maintained through convalescence. It may not be advisable to enforce such a drastic undernutrition but overfeeding must be avoided.(52)

Shock and vomiting--with hold food completely. If no engorgement of the lungs and systemic veins, I.V. glucose in hypertonic solutions may be given. This may aid nutrition of the heart by increasing the coronary flow.(155) After vomiting is over, one can give glucose liberally orally.

Drugs--Oxygen is given in concentration of 50 to 60% as advocated by Baroch and Levy(156) to be used in cyanosis, marked dyspnea, and pain not relieved by morphine. Use for 5 days and discontinue if improvement is noted. It is important to lower the concentration gradually when withdrawn.(52)

Aminophylline--given orally and I.V. widely is employed but its value is open to question. Experimentally it did not exert any influence favorable to the course of infarction.(157,158) The purine derivatives are in much greater favor in Europe than in Americ, but their favor is increasing here. It is now generally conceded that they have a dilating influence on the coronary arteries and increase the coronary flow. Smith, in experimental work, demonstrated a much greater coronary flow with Euphyllin than with the other members of this group, equal to that of nitroglycerine. The preponderant clinical opinion warrants their extensive use.(13)

Digitalis--In the therapy of coronary thrombosis is contraversial.(154) (159,160,152,161) The majority of experimental studies(162) indicate it causes slight constriction of coronary vessels and retards coronary flow. In congestive failure the improvement of cardiac function compensates for its constrictive effect. Tishberg, Hitzig and King(163) in clinical study fo 59 patients with myocardial infarction suggests use of digitalis in myocardial infarction can be determined by prevailing type of failure. In congestive failure, cautious use of digitalis is probably helpful. It is practically universally conceded that digitalis has no place in the treatment except when complicated by congestive heart failure, or persistent rapid, auricular fibrillation.(13)

Nitrites- are of no value in coronary occlusion and may tend to increase the size of the infarction.(152,164, 165,166)

Ephedrine--itsuse appears paradoxical. Levine, Ernstene and Jacobsen(167) have shown that in patients subject to anginal pain, an attack can be induced with use of epinephrine injected I.M. or I.V. EKG changes are similar to angina and coronary occlusion are obtained.(168 159) However Levine(41) has used it frequently in heart block complicating coronary occlusion using 0.3 to 0.5 cc. of adrenalin each

hour for 48 hours with disappearance of the tendency to syncope. It is best used only in emergencies as in extreme shock or cardiac standstill. Caffine Sodium Benzoate and adrenalin have a very restricted, carefully scrutinized use in the treatment of extreme shock, but certainly not at any other phase(13)

Quinidine--found useful in the treatment of paroxysmal ventricular tachycardia(170) although it tends to disappear spontaneously it may persist presenting an important therapeutic problem. This drug appears to be the only one that will control this condition. The dose varies from 5 gr. to much larger doses. Some advise the routine use of small doses of it as a prophylactic for this condition. However, as this is a myocardial depressent it had better be reserved for a definite indication.(13)

Sex Hormones--Estrogen has a vasodilating effect. Considerable evidence has been collected by Gilbert in support of the vasomotor mechanism, as an etiological factor in coronary artery disease.(138 This article deals with a group of patients with coronary artery disease who showed remarkable improvement clinically while under going treatment with sex hormones. In 1938 and again in 1940,

Scherf(139) has pointed out an effect of hypo-ovarianism on coronary artery and myocardium in certain women. He believes these changes are the result of a deficiency of ovarian follicular hormone and not by rest, vasodilation and sedatives. Master, Jaffe, and Dack (140) used 16 drugs and placebos on coronary artery disease and found no drug gave a specific effect and obtained the best effect with a placebo.( 132)

Therapy of Myocardial Insuffiency

With the exception of especial care concerning the use of digitalis, already discussed, the management of myocardial insuffiency of coronary origin does not differ in any essential respect from the treatment of congestive failure due to any other cause. In the acute attack, morphine is best in plethoric individuals while venesection is helpful. I.V. Aminophylline is widely advocated. After the acute attack is controled, the continued use of digitalis is believed to be the most effecient means of restoring function of the right ventricle and preventing acute paroxysms of dyspnea. Best results from slow complete digitalization followed by a maintanence dose of approx. 1½ gr. of powder-leaves are obtained. Although use of digitalis

has been stressed(171) it is obvious that the importance of this therapy is not generally appreciated and its renewed emphasis at this time is justified.(40)

Convalescent and permanent management

Convalescence is still mor difficult to Parkinson's advice is particularly applicable here, "we should explain to the patient a little about the nature of his 'heart attack.' I say 'heart attack' because it is unjustifiable where such issues are involved to be a party to any policy of hood winking or allowing the attack to be regarded as anything else." (133) However as Stevens points out, one should try to re-establish the patient with his disability and not increase his invalidism. (134)

After the bed rest of about 6 weeks, and a convalescence of two or three months, an inventory of the physical assets and the liabilities must be taken. For some, the only handicap necessary is to avoid strenuous physical exertion, such as climbing stairs, changing tires, etc. For others it means relinquished ambitions or retirement. However, a useful and happly life not greatly shortened, if at all, is much more frequent than was assumed in the past. In cases with Diabetes,

during the acute stages of occlusion, insulin is hazardous on account of the danger of lowering the blood pressure and should be used but rarely(13)

Surgical Considerations

In closing it is desired to call attention to recent progress in the surgical treatment of coronary disease. As yet such treatment is reserved for desperate cases where relief cant be obtained medically. Of the various surgical procedures, paravertebral alcohol injected in the 4 or 5 upper dorsal sympathetic ganglion is definitely established as a reasonably safe and highly effective in a number of cases.(172,173) J. C White describes the method of performaing these injections in a well explained and illustrated article.(172) Total thyroidectomy for the relief of coronary pain(174) and development of a new blood supply to the heart by grafting tissues(pectoral muscles or omentum) onto the myocardium(178) are still in the experimental stage.(175,176,177) The latter method is particularly promising.(179,180,181,182) Beck(40) performed this operation on 25 persons. In 14 cases the mortality was 50% and in the last 9 cases, no fatalities occured. He clains all patients improved with reduction of pain and increased tolerance to exercise. Three patients have been completely relieved of pain and consider themselves cured.(40) It has been shown that it is possible to deliver a sufficient quantity

of blood thru occluded arteries by surgical means to prevent death of the myocardium and ventricular fibrillation. Ultimately these two destructive factors decrease as a common coronary bed becomes into existance.

Another method by which the coronary artery bed can be produced is by inflammation, either mechanically or chemically. Beck uses abrasion of the surface of the heart by powered beef bone as foreign body to produce inflammation. This is shown to reduce the mortality from 70% to 50%(141), in normal hearts with ligation of the coronary artery, at its origin following abrasion previously. Abrasion opened the inter-coronary communications and decreased the size of the infarct: in some, no infarct developed but it always occured in the normal hearts. Calcium and magnesium(as silicates) in fibrous form have also been used(142)

## SUMMARY

And so. in the confines of this all to brief paper, an attempt is made to form a summary of the accumulated information upon this vital and increasing important subject: coronary thrombosis. This attempt is probably justified from the fact that in years recent, the conviction has been growing that the incidence of coronary heart disease the world over has been continually increasing and that physicians are among the most frequent victims.

The coronary circulation and its relation to heart disease has been the subject of intensive study by anatomist and cardiologists during the last 20 years. Heberdin, in 1763, so accurately described angina pectoris that nothing has been added to its clinical description. From that time to nearly the present, the occlusion of the coronary circulation has been grouped with angina pectoris representing the severe type. Hammer, in 18 78, placed the first antemortem diagnosis of coronary occlusion on record. Dock(in 1896) reported the first american case. Credit for initiating our present conception of coronary thrombosis belongs to Herrick. The clinical recognition is largely due to the emphasis given to it by American authors. It has even been suggested that it may be more common in America.

It has been shown since the time of Spalteholz, in 1907, that the coronary circulation is not by end-arteries, but that there are extremely rich anastomotic beds between the branches of the coronary arteries. There are good anastomosis everywhere in the heart except in the right auricle and the auricular septum.

Among the contributing factors, prolonged mental strain has been emphasized. It has been shown by Boss and Donner that this is not entirely true since it is as common in working classes. Tobacco is frequently with some unanimity of opinion, incriminated as a factor. Syphilis does not involve the coronary arteries. The all important disease of these vessels is arteriosclerosis. Diabetes tends to indicate the type of individual apt to suffer from coronary disease. Hereditary factors, although extremely difficult to analyze, is most important especially in those persons having the disease at a young age. The average age is 57.8 years with females somewhere around 6 years later than males.

The typical clinical picture of acute coronary thrombosis was discussed in detail. In addition certain atypical features were emphasized that in some instances resembles an acute surgical abdomen. There is commonly a fall in blood pressure. The important features on ex-

amination are shock, distant heart sounds, gallop rhythm, the development of various irregularities in heart rhythm, occasional pericardial friction rub, rales in the lungs and sometimes an engorgement of the liver. The urine frequently contains sugar and albumen and casts, at times oliguria or suppression of urine. The important conditions that at times have to be considered in differential diagnosis were an acute surgical abdomenal condition, angina, pneumonia, diabetic acidosis and finally so called chronic myocarditis. The proper diagnosis in most cases is possible, although all methods including EKG may be necessary. The EKG findings are quite characteristic in coronary occlusion with elevation, depression or rounding of the RS-T segment, low amplitude, and prominent Q wave in lead III. The diagnosis should be made clinically and supported by the EKG and not by it alone.

The pathological picture of coronary thrombosis is variable, depending on the size of the occluded vessels and the rate of occlusion. If the smaller vessels are occluded, the acute eposodes do not occur. The most frequent site of occlusion has been considered to be the anterior descending branch of the left coronary but findings of some men do not bear this out, finding it about equally in the right and left.

The criteria for prognosis is most unsatisfactory. In general 50% have immediate recovery. Slight differences in the mortality were found in analysis of age and sex, development of pericarditis, and auricular fibrillation. Ventricular tachycardia and heart block seemed to have a greater mortality than the average. Even the type of EKG has no influence on whether the patient would recover or not.

The question of treatment for the present must be based partly on theoretical grounds as there are no data available to compare end results of one regime with those of another. The acute and rapid character of the disease often makes our deductions as to therapy fallacious, because frequently many drugs are given in a short time and it is difficult to appraise the proper value of any single one. A proper understanding of the pathological process going on during thrombosis will help to some extent in rationalizing therapy. In the acute stage, morphine and rest are essential. Other means of therapy were discussed. It appears that up to the recent time treatment was merely palliative and symptomatic, and other than rest, there were no factors of prophylaxis or cure. Recent surgical procedures point favorably to this end, by developing a new blood supply to the heart by grafting tissues onto

the myocardium or by developing inflammation thru some abarsive substance or by irritating material with ultimate increase of caoillary bed and inter-coronary communications.

The disease today, is well recognized, nearly always easily diagnosed; the difficult cases are usually differentiated by the following:

1. Muffled heart sounds, gallop rhythm, alternating pulse
2. Previous history of "indigestion" on exertion
3. Tightness of chest
4. Radiation of pain not typical for abdominal disease
5. More apt to have dyspnea with coronary disease
6. Pain: Rarely epigastric alone, but also substernal
7. Age: Victims of coronary thrombosis preponderately elderly men.
8. Electrocardiogram fairly typical.

The pathology is recognized and often predicted ante-mortemly as to presence and location, while the prognosis is difficult if not impossible to make. The treatment is far from satisfactory. Perhaps through follow up of the promising recent surgical procedures, our ability to compete with this disease will develop to such a state that coronary thrombosis will no longer be a major threat to the lives of mankind.

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