Origins of a clinical concept of coronary thrombosis: a study in medical history of heart diseases

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The Origins of a Clinical Concept of Coronary Thrombosis: A Study in Medical History.

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I

The history of the clinical recognition of coronary thrombosis is inseparably bound up with that of angina pectoris. The accurate separation of the one from the other has been an achievement of the twentieth century. The facts upon which this achievement rests are not, in the light of a review of the older literature, of such recent origin.

It is the clinical picture of acute and relatively sudden thrombotic obstruction of one of the major branches or trunks of the two coronary arterial trees, which still stands as our most helpful type in the consideration of coronary disease. This picture, so vividly drawn for us by Dr. James B. Herrick, is one of "severe, enduring, substernal or epigastric pain, unprovoked by effort, and attended by shock, lowered blood pressure, disordered and weakened heart condition, dyspnea, fever, leucocytosis, pericardial rub, embolic complications; with death in a few hours or days from ventricular fibrillation or rupture, or with partial or complete recovery after a slow convalescence" (1). It is the history of the recognition of this particular clinical entity, to
which the term coronary thrombosis is best applied, which will be traced in the following pages.

Coronary thrombosis is not a new disease. It is its ante mortem diagnosis and the synthesis of the facts upon which this diagnosis depends, which is new. The older clinicians and writers, Osler (2), Allbutt (3), Mackenzie (4), and others of their generation, regarded many cases as angina pectoris which we would now readily diagnose as coronary thrombosis. Prior to the classical delineation in 1768 by William Heberden (5) of the archetype of true angina pectoris, physicians were confronted with patients who presented syndromes of cardiac pain which, as we shall see, were variously misinterpreted but which even then were sometimes recognized as cardiac in origin. Whether the incidence of sudden and acute coronary thrombosis has markedly increased during the past quarter century from what it was in Osler's day cannot be surely determined. A fortiori, the problem of determining the frequency of the condition in antiquity, before the publication of the De Sedibus et Causis Morborum by Morgagni in 1761, as well as before the publication of Herrick's memorable series of clinical studies in the decade 1910-1920,
is one which must go unsolved for lack of evidence (1). One naturally wonders whether the striking prevalence of coronary thrombosis today is due so much to an actual increase in its frequency as merely to the fact that it is now recognized more certainly and more readily.

It was held up to the time of Hippocrates (460-377 B.C.) that the heart could not be diseased (6). In the literature of antiquity the first notable allusion to heart disease occurs in the De re medicina of the Roman medical writer Aurelius Cornelius Celsus (7) who lived in the reign of Tiberius (14-37 A.D.). Here Celsus speaks for the first time of a puzzling disorder known to the Greeks as kardiakon, and called by the Romans Cardiacus or Morbus Cardiacus. According to Dr. Phillip S. Roy (6) this disorder consisted of "an indefinable and incoordinated group of symptoms — profuse sweating, fever with thin, weak pulse and short, panting respiration, great bodily weakness with cold extremities", and it was attributed to the heart or stomach. The justly famous Greek clinician, Aretaeus the Cappadocian, who lived either under Domitian or Hadrian (2d to 3d century A.D.) refers to this condition as
"syncope" and regards it as a definitely cardiac affection. Galen (131-201 A.D.) mentions it and regards it as a general weakening disease involving both the heart and the stomach. The Byzantine physicians Aetius of Amida and Alexander of Tralles who lived in the sixth century A.D. describe this condition as a gastric disorder. The accepted treatment, we are told, was roborant and the universal remedy was wine.

Following the mention of this disease by Aetius and Trallianus it disappears from the literature, according to Roy (6), for the next six centuries. It is mentioned by Chaucer (1340-1400) in the Canterbury Tales in the following quaint passage which William Osler used for a frontispiece in his Lectures on Angina Pectoris and Allied States (1897) (2):

"But wel I woot thou doost my herte to erme
That I almost have caught a cardiale."

It seems to one familiar with our modern concept of coronary thrombosis that the above historical facts may quite possibly be the first adumbration of the clinical appearance of this disease to be found in medical writing. Roy (6) states that in 1835 Seidlitz of St. Petersburg
identified this kardiakon or Morbus Cardiacus of the ancients with exudative pericarditis, and that Landsberg in his account of the ancient conception of cardiac diseases (1847) regarded it as a secondary anemia. It should be pointed out that neither of these men wrote at a time when a clinical idea of the signs and symptoms of coronary thrombosis sufficient to make a reliable ante mortem diagnosis was in existence. It is submitted that the likeness between this disease of antiquity and the coronary thrombosis of today is such as to support strongly the possibility of their identity.

In the consideration of the very limited available material pertinent to our subject during a period which extends from Graeco-Roman times, through the Byzantine period, the Mohammedan and Jewish periods, the Middle Ages, and well into the period of the Renaissance, the Revival of Learning, and the Reformation (1453-1600), two further matters remain for our discussion. The first concerns the fact that the Roman Stoic philosopher, Seneca (c.3 B.C.-65 A.D.), appears to have had angina pectoris. In his Epistolae ad Lucilium he gives a graphic account which is in part as follows (2):
"The attack is very short and like a storm. It usually ends within an hour. I have undergone all bodily infirmities and dangers; but none appears to me more grievous. Why not? Because to have any other malady is only to be sick; to have this is to be dying."

Seneca states further that the disease which he had was called by his physicians a meditatio mortis. One can't help wondering whether the consummation of such "meditations of death" might not have been a fatal attack of coronary thrombosis.

Finally, we must mention that British scholars (8) have been pointing out for a good many years now that, contrary to general usage, the i in angina is short and not long and that the accent is accordingly on the first and not on the second syllable. The proof of this claim they find in the scansion of one of the plays, Trinummmus, of the Roman comic poet Plautus (d. 184 B.C.).
II

It is not generally known that William Harvey, the great English anatomist and physiologist (1578-1657), who discovered the circulation of the blood, must also be credited with reporting a case which now appears almost certainly to have been one of coronary thrombosis (9). The account appears in his Second Disquisition to John Riolan, Junior, was written about 1650, and may be regarded as the first reported case recognizable with reasonable certainty as one of acute coronary obstruction to be found in medical history. The patient, "a noble knight", did not recover as his cardiac infarction terminated fatally with ventricular rupture, a fact which helps us perhaps more than Harvey's scant clinical narrative in making the diagnosis. As probably the earliest recorded case of coronary thrombosis it deserves to be quoted:

"A noble knight, Sir Robert Darcy, an ancestor of that celebrated physician and most learned man, my very dear friend Dr. Argent, when he had reached to about the middle period of life, made frequent complaint of a certain distressing pain in the chest, especially in the night season; so that dreading at one time syncope, at another suffocation in his attacks he led an unquiet and anxious life. He tried many remedies in vain, having had the advice of almost every medical man. The disease going on from bad to worse, he by and by became
cachectic and dropsical, and finally, grievously distressed, he died in one of his paroxysms. In the body of this gentleman, at the inspection of which there were present Dr. Argent, then president of the College of Physicians, and Dr. George, a distinguished theologian and preacher, who was pastor of the parish, we found the wall of the left ventricle of the heart ruptured, having a rent in it of size sufficient to admit any of my fingers, although the wall itself appeared sufficiently thick and strong; this laceration had apparently been caused by an impediment to the passage of the blood from the left ventricle into the arteries" (10).

It is a pardonable heresy in the light of modern knowledge to regard this ventricular rupture as the outcome of cardiac infarction due to coronary thrombosis, although Harvey evidently did not interpret it as such.

The case of the father of Edward Hyde, 1st Earl of Clarendon (1609-74), also appears to have been one in which death was due to a fatal coronary thrombosis following a history of typical sporadic anginal episodes. Dr. Ralph Major (11) in his medical anthology, Classic Descriptions of Disease, quotes the lengthy account of this case taken from The Life of Edward Earl of Clarendon, (Oxford, 1857). The fact that this book is an autobiography and that its writer died in 1674 would seem to establish the account of the father's death as perhaps the second earliest recorded case of coronary thrombosis; however the great age of the patient at the time of the final
seizure (he was seventy), and the earlier frequent bouts with angina of effort, as well as the almost instantaneous death and its attendant circumstances, make the case seem somewhat atypical. Moreover, the narrative was not written by one with medical training.

One has only to glance at the splendid illustrations in the magnificent *De Fabrica Humani Corporis* (1543) by Vesalius to realize that at the time of his death (1564) the study of human gross anatomy had become much as it is today — "a living, working science". It remained for one of the post-Vesalian anatomists, a professor at Montpellier, Raymond Vieussens (1641-1716), to give the first correct description of the coronary arteries (7). Thus a foundation was laid for morbid anatomy in general and for cardiac pathology in particular. Giovanni Battista Morgagni (1682-1771) availed himself of this foundation so effectively that it seems almost an understatement to refer to him as the father of pathology. Garrison comes closer to the truth when he says (7) that the *De Sedibus et Causis Morborum* in which Morgagni in his seventy-ninth year published the results of his life-work, "constitutes the true foundation of modern pathologic anatomy, in that, for the first time, the records of postmortem findings
are brought into correlation with clinical records on a grand scale."

Sir William Osler, like certain other prominent clinicians of his era, regarded a post mortem diagnosis of coronary thrombosis as compatible with and probably etiologically related to an ante mortem diagnosis of true angina pectoris (2) (12). Nevertheless the classic picture of angina pectoris to Osler and his contemporaries as well as to their teachers is the clinical concept which the best parlance of modern medicine refers to as **Heberden's angina** or **angina pectoris of effort** or more commonly as just plain angina pectoris. We must now trace for some distance the history this symptom complex has in all fairness and quite understandably carved out for itself, for it is from this syndrome that a later and more conscientious correlation of pathological findings with clinical signs and symptoms was able to evolve the differential diagnosis which now makes coronary thrombosis an easily diagnosable disease.

We have Osler's word, well-documented, that to Morgagni is due the credit for the first description in medical annals of a single case of angina pectoris vera (2). This description appears as Case V of that section of the **De Sedibus** devoted to aneurysm of the aorta. Osler read extracts from
the case to the graduate class in medicine at the
Johns Hopkins Hospital, circa 1895, and the clinical
portion of Morgagni's account is as follows:

"A lady, forty-two years of age, who for a
long time had been a valetudinarian, and
within the same period, on using pretty quick
exercise of body, she was subjected to attacks
of violent anguish in the upper part of the
chest on the left side, accompanied with a
difficulty of breathing and numbness of the
left arm; but these paroxysms soon subsided
when she ceased from exertion. In these
circumstances, but with cheerfulness of
mind, she undertook a journey from Venice,
purposing to travel along the continent,
when she was seized with a paroxysm, and
died on the spot. I examined the body on
the following day" (13).

In his autopsy report Morgagni does not mention
the state of the coronary arteries although he
does speak of induration of the aortic valves and
of ossification of the inner surface of the aorta.
One wonders what this great pathologist found in
the coronary arteries and whether he took care to
examine them carefully or at all. Having no
precedent he can hardly be blamed if he failed to
examine them.

Despite the earlier appearance of this rather
brief sketch by Morgagni and of the longer but no
more informative recollections in the memoirs (1632)
of the Earl of Clarendon, it is undoubtedly the
classic account of true angina pectoris by the distinguished English practitioner William Heberden (1710-1801), of London, which put the disease on a firm clinical basis. The main outlines of his picture of the disorder were first sketched by him in a paper entitled *Some Account of a Disorder of the Breast* which he read on July 21, 1768 before the Royal College of Physicians and which was subsequently published in vol. ii of the *Medical Transactions* of the College of Physicians, 1772 (2) (14). The following extract from the original description should be quoted:

"There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it . . . The seat of it and sense of strangling and anxiety with which it is attended may make it not improperly be called angina pectoris.

"Those who are afflicted with it are seized while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away if it were to increase or to continue; the moment they stand still all this uneasiness vanishes. In all other respects the patients are at the beginning of this disorder perfectly well, and, in particular, have no shortness of breath, from which it is totally different" (2) (14).

A fuller account of Heberden's experience with angina pectoris was later set down by him in his
Latin Commentarii (London, 1802) which were later translated by his son, William Heberden Jr., as Commentaries on the History and Cure of Diseases (15), and which became widely and deservedly popular. In this later work Heberden adds such notable details as the age and sex incidence and the typical distribution, onset and recess of the pain and contrives to make his narrative so vivid that it has not since been improved upon.

Sir Humphry Rolleston (8) states that a single case of angina pectoris, "de spasmo praeordiali a motu corporis", was recorded by the German physician Friedrich Hoffmann in 1734. Heberden's later account, however, shows that, all told, Heberden had seen a hundred cases (8). The French claim priority in this matter of original descriptions of the angina of effort, for one of their countrymen, M. Rougnon, professor of medicine at the University of Besancon who on "le 23 Fevrier, 1768" wrote a letter published the same year describing a case seen by him which scholars have since had some difficulty in regarding as one of angina pectoris (16). The matter would seem to have been settled in a recent lengthy article by Hans Kohn of Berlin entitled Zur Geschichte der Angina Pectoris. Heberden oder Rougnon? (17) in which he shows that Rougnon's case
was one of pulmonary emphysema, with dyspnea and cardiac dilatation, and not angina pectoris.

Edward Jenner (1749-1823) may be said to be the first physician to definitely correlate the autopsy findings of coronary artery disease with the clinical picture of angina pectoris (2) (8). Rolleston adds to this the statement that "it is possible that John Hunter, on whose account, as his anginal symptoms dated from 1773, Jenner kept silence, knew or suspected this association of coronary disease with angina in 1776 when John Fothergill published a fatal case of angina in which at the post-mortem Hunter found that "the two coronary arteries from origin to many of their ramifications on the heart were become one piece of bone" " (8).

Heberden was the recipient of a letter from Jenner written in 1776 in which Jenner gives his diagnosis of John Hunter's case and suggests "for the first time, the probable association of disease of the coronary arteries with angina pectoris" (2). Osler, throughout his life held to this Jennerian view, and he often demonstrated, as De Graff points out, coronary thrombosis at autopsy in patients who during life were good examples of the classical
picture of angina pectoris (18) (2) (12). The views of Jenner were communicated by Jenner to his colleague Caleb H. Parry (1755-1822) and thus were ultimately published in the latter's paper "An Inquiry into the Symptoms and Causes of the Syncope Anginosa, commonly called Angina Pectoris; illustrated by Dissections" which although read before a small medical society in 1788 was not published until 1799 (8) (19). With this exception we must look to Jenner's personal correspondence for the little we possess concerning his highly original but eminently sound notions of the relation of coronary artery disease to angina pectoris.

The ultimate triumph in recent years of the Jennerian and Oslerian view that true organic or major angina pectoris is predominantly due to disease of the coronary arteries over such distinguished opposition as that of Laennec, Corrigan, Mackenzie (4), Allbutt (3) and others is due in part to improved pathological technique, partly to a more careful attention to the correlation of pathological findings with clinical evidence, partly to Allen Burns' great theory of intermittent claudication as an explanation of
the causation of angina pectoris by coronary disease (2) (8). The present strong prevailment of this view that coronary occlusion of a partial or almost complete character, not too sudden or acute in its onset, may frequently cause a typical case of angina pectoris vera, is also due to the study, research, and understanding caused by the realization a relatively few years ago that thrombotic occlusion of a coronary artery is not hard to diagnose before death and that a patient may even recover from such a blow.
III

Adam Hammer (1818-1878), a St. Louis physician and surgeon of German birth and training, is generally credited with the first correct ante mortem diagnosis of coronary thrombosis (20). He reported his case in the Wiener Medizinische Wochenschrift in 1878, the last year of his life. The article has been translated and abstracted by Major in the latter's anthology (11). The case seems to have been somewhat atypical but the following remarks by Hammer are worth noting:

"What impressed me particularly about this case and attracted my attention in the highest degree, was the sudden appearance and the steadily progressive course of the collapse. I thought that only a sudden, progressively increasing disturbance in the nutrition of the heart itself such as a cutting off of the supply of nourishment could produce such changes as this case showed, and that such an obstruction could be produced only by a thrombotic occlusion of at least one of the coronary arteries. From lack of ground for any other satisfactory explanation, I was carried away by this thought. . .

"I mentioned my conviction to my colleague at the bed side. He however had a non-plussed expression and burst out "I have never heard of such a diagnosis in my whole life." and I answered "Nor I also." "

In 1884 the German clinician Ernst von Leyden published an article on sclerosis of the coronary arteries (21) in which he mentions in passing the case of Hammer's patient and of the Danish sculptor, Thorwaldsen, as examples of what may ensue, namely,
sudden death, from the sudden deprivation of a major portion of the blood supply of the myocardium. He reports a few cases in which a coronary thrombus was found at autopsy and from the appended clinical histories a few of the signs and symptoms which we now know to be part of the picture of coronary thrombosis are seen to be included. The article is primarily concerned with cases of coronary sclerosis without attendant thrombosis.

George Dock (b. 1860) may perhaps be regarded as the second physician, certainly the second American physician, to report an instance of coronary thrombosis diagnosed ante mortem and confirmed by autopsy. In his article Some Notes on the Coronary Arteries (22) published in 1896 he is found to be among the first to recognize the importance of the pericardial friction rub as an aid in the diagnosis. Speaking of Dock's article the contemporary cardiologist Samuel Levine in an extensive review of the clinical features of coronary thrombosis, has this to say:

"At the time of his publication one would judge from the account it contains that the other important features that make up the clinical picture of coronary thrombosis were not thoroughly known; at least, it is surprising that further papers did not appear by the same author to emphasize the importance of recognizing this clinical entity" (23).
In 1897 appeared the monograph of the French pathologist Rene Marie on Infarct of the Myocardium (24), a splendid work which ably described the post mortem changes of coronary thrombosis but which failed to present any clear-cut clinical symptomatology with which post mortem changes could be associated (23). The same criticism applies to the monograph by Sternberg on Partial Aneurysm of the Heart which appeared as late as 1914 (1). With respect to such works Herrick says (1) that they are "teeming with records, the clinical significance of which was overlooked because the vision of the writers as of the readers was focused on the pathology." The same criticisms apply to the treatise by Henri Huchard (24) on Diseases of the Heart and the Aorta.

Ludolph Krehl of Greifswald, Prussia, in a short sketch on occlusion of the coronary arteries written for the Nothnagel Encyclopedia (25) (1901) made mention of the fact that recovery following an attack of coronary thrombosis was possible. He also stressed the fact that the symptomatology was more apt to be severe if the vessels were suddenly occluded than if the occlusion grew out of a diffuse and gradual coronary sclerotic process.
In 1910 two Russian internists, W.P. Obratzow and N.C. Straschesko published an article which is rightly considered by such modern authorities as Herrick and Levine to be "the first important and satisfactory account of the clinical features attending attacks of coronary thrombosis" (23). This article, Zur Kenntnis der Thrombose der Coronarterien des Herzens, appeared in German in the medical journal Zeitschrift fur Klinische Medizin (26).

The article emphasized a triad of symptoms which were to be looked for in making the diagnosis of coronary thrombosis during life. This triad comprised 1) severe and lasting retrosternal pain; 2) dyspnea and orthopnea; and 3) gastralgia. A series of three cases was presented and the correct ante-mortem diagnosis, according to Levine (23), was made in two of the three cases. All three of the cases had an antecedent history of angina pectoris. These two Russian authors also called attention to such features now regarded as important in the clinical diagnosis of coronary thrombosis as 4) gallop rhythm; 5) Cheyne-Stokes breathing; 6) pericardial friction; 7) distant heart sounds; 8) mural thrombi; and 9) pale cyanosis. In one of their cases fever
was present and this they ascribed to a concomitant pericarditis and pleuritis. They noted too that softening and rupture of the infarcted area might set in along with hemopericardium; and they were aware that the clinical and pathological course which followed the onset of the thrombosis was, other things being equal, a function of the size of the coronary artery occluded.

The same year in which this article appeared Sir William Osler in his Lumleian Lectures on Angina Pectoris, delivered before the Royal College of Physicians of London, made it clear that he had often found coronary thrombosis associated with pericarditis and ventricular rupture in autopsies on his cases. Careful reading of these lectures (12) today shows that he did not correlate these post mortem findings with any clinical entity more definite than a "severe" type of angina pectoris. One hesitates to criticize the scientific thoroughness of one whose imperfections, clinical and otherwise, were so few, yet here is one instance where it appears that Osler missed a trick. He was not alone of course. Sir James Mackenzie in his last work on angina pectoris published as recently as 1924 (4) gave no fact to show that he had diagnosed the
condition clinically in his practice (23).

The year after the splendid presentation for the first time in the literature of a fairly clear and well-defined outline of the clinical findings in coronary thrombosis by Obratzow and Straschesko, an article appeared in the Deutsche Medizinische Wochenschrift (27) by the German clinician Hochhaus which reported four cases of coronary thrombosis of which two were correctly diagnosed during life.

For some reason these two articles did not create a response in Europe which led to any extensive further study and subsequent frequent diagnosis of coronary thrombosis either in Germany or any of the other countries of Europe. In his Harvey Lecture on The Coronary Artery in Health and Disease (1) which Dr. Herrick delivered in 1931 at the age of seventy, he remarked that "in Europe, where a comparatively tardy interest has been manifested, writers still refer to it (coronary thrombosis) as rare. It is plain that what we look upon as acute infarction is either not so common in Europe as in this country or is classed as some other affection, perhaps angina pectoris." One is reminded of Osler's quotation from William James wherein the American and European ways of life are contrasted (28):
"Neither the nature nor the amount of our work is accountable for the frequency and severity of our breakdowns, but their cause lies rather in those absurd feelings of hurry and having no time, in that breathlessness and tension; that anxiety of feature and that solicitude of results, that lack of inner harmony and ease, in short, by which the work with us is apt to be accompanied, and from which a European who would do the same work would, nine out of ten times, be free."

Whatever the explanation, the greater portion of the rest of the modern clinical concept of coronary thrombosis has been worked out in the United States. The process has centered largely about the work of Dr. James B. Herrick and has taken place for the most part during the years from 1912 to 1920 inclusive. During this period Dr. Herrick was professor of medicine at Rush Medical College. He was familiar with the clinical and pathological contributions of the past and with the work, for example, of Obratzow and Straschesko and possessed a thorough knowledge of the anatomy and pathology of the coronary circulation. He also had adequate clinical material at Rush upon which to base his observations.

In December, 1912, he published in the Journal of the American Medical Association his first article on the subject, Clinical Features of the Sudden Obstruction of the Coronary Arteries. He pointed out
that the dictum of the German pathologist Cohnheim (1839-1884) that the coronary arteries are end-arteries had been disproved by such workers as Spalteholz and Hirsch. He cited evidence tending to prove that not only are there non-negligible anastomoses between the various branches of the coronary arterial trees, but that these anastomoses may become functional even under somewhat acute occlusive conditions. Referring to the work of Porter and of Miller and Matthews in ligating the coronary arteries of dogs, he concluded that "Experimentally, sudden death, even late death, is not a necessary consequence of obstruction of even large branches, such as the descending branch of the left coronary artery" and that "There are numerous autopsy observations, frequently with helpful clinical history, that show directly or by inference the existence of efficient anastomoses, and the ability of the heart at times to survive the obstruction of a coronary or some large branch." Thus he emphasized the fact that coronary thrombosis need not necessarily end fatally.

He also reported two cases in this article, cases in which as he said the coronary thrombosis gave symptoms which "are severe, are distinctive enough to enable them to be recognized as cardiac,
and in which the accident is usually fatal, but not immediately, and perhaps not necessarily so." His account of the first of these cases, that of a man, aged 55 (29) has become the classic description of the clinical picture of coronary thrombosis which we recognize today. Major quotes it as such (11). It is too long to be given here but the following typical features are found to have been presented by the patient: 1) severe, prolonged pain not associated with effort located in the lower precordial region; 2) nausea and vomiting; 3) slight fever some time after the onset of symptoms; 4) a rapid thready pulse; 5) dyspnea; 6) slight pulmonary edema; 7) feeble heart sounds; 8) slight albuminuria; 9) restlessness and inability to lie quietly in bed; and 10) death (not a necessary consequence) about two days after the onset of the pain, from circulatory failure.

Another article by Herrick does not appear on this subject until 1918 but in 1916 the eminent New York internist, Dr. Emanuel Libman in an open discussion on the various kinds of precordial pain stressed the fact that the diagnosis of recent coronary thrombosis can often be made easier by the development of a slight temperature and a moderate leucocytosis, as well as
by a patch of pericarditis, all three of them coming on within two days after the onset of the severe pain (30).

In 1918 Levine and Tranter (31) published an article calling attention to "Infarction of the Heart Simulating Acute Abdominal Conditions". However, both Herrick and Obratzow and Straschesko in their initial contributions to the subject of coronary thrombosis warned against the possible confusion of the condition with one of the acute surgical disorders of the upper abdomen as well as of the abdomen generally. Herrick's second article, appearing in 1918, deals specifically with angina pectoris (32) but emphasizes the role of gradual coronary occlusion in the etiology of angina pectoris and the differential diagnosis between angina pectoris and coronary thrombosis. A third publication by Herrick, Concerning Thrombosis of the Coronary Arteries (33), May, 1918, emphasizes that most of the patients are middle-aged or elderly men and that while heart and bloodvessels may show evidences of arterial and cardiac sclerosis, and the blood pressure be high, there are other cases in which no sign of such changes can be made out.

Especially during the years 1918 to 1920, inclusive, as well as since that time, electro-
cardiograms have been shown to present rather pathognomonic changes in cases of coronary thrombosis. In the discovery of these changes Herrick and his pupil F.M. Smith have been prime movers. In 1918 Smith (34) published his experimental observations upon electrocardiographic changes following the ligation of the coronary arteries in dogs. He noted sharp inversion of the T wave of the electrocardiogram in dogs a short time after the coronary arteries were ligated. Shortly after the publication of Smith's first article, Herrick (1919) (35) published an account of the first case of coronary thrombosis which was proved by post-mortem examination, with electrocardiograms which showed in leads I and II sharp inversion of the T waves similar to those obtained by Smith in his experiments with dogs. Herrick also noted at this time that ten days later the T waves were less negative and that in five months curves of low amplitude were shown by the tracings. In commenting upon this work by Herrick, Levine (23) remarks that "at this time the more characteristic changes that are found in human electrocardiograms during the first few days after an attack of coronary thrombosis were not fully appreciated but the above work served as a forerunner of the contributions that followed."
In 1920, H.E.B. Pardee announced his valuable discovery that during the days immediately following an attack of coronary thrombosis fairly characteristic changes may be noted in the electrocardiograms (36). These changes consist of a high take-off of the T wave from the descending limb of the R wave plus the fact that during the subsequent days the T wave goes through rapid changes and may even become inverted. In commenting on the value of these changes Levine states that "in some of our case histories there are instances in which this electrocardiographic sign may be the single definite evidence that distinguishes the condition and that differentiates it from other entirely unrelated possibilities like gall stones or gastric ulcer."

Following this work by Pardee numerous other articles have appeared which have elaborated and confirmed our knowledge of the electrocardiogram in coronary thrombosis.

The articles of Levine and Brown (1929) (23) and of J.T. Wearn (1923) (37) are valuable and scholarly summations of current knowledge concerning coronary thrombosis at the time of their appearance. Since their publication the clinical picture whose historical evolution has been traced in these pages may be said to be essentially unchanged.
References Cited


30. Libman, Emanuel.: Remarks concerning a paper on precordial pain, Medical Record (N.Y.), 89:124, 1916.


37. See No. 10., op.cit.supra.

Corrigenda: Reference No. 23., should be changed to read as follows: Levine, S.A., and Brown, C.L., Coronary Thrombosis: Its Various Clinical Features, Medicine, 8:245-418, 1929.