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Electrocardiographic diagnosis of myocardial infarction

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THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF MYOCARDIAL INFARCTION

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INTRODUCTION

The cardiovascular apparatus may be looked upon as a device essential to the maintenance of homeostasis. This it achieves by a series of adaption and protective reactions. Many of these reactions evoked by assaults or threats are operated at great cost to the organism, a matter of small moment except for transient symptoms if the parts are strong and the stress of short duration. Should, however, the adaptive and protective patterns be maintained unduly long or the reacting organ be weak, or already operating under strain, or should the protective reactors exert an additive effect with other stress, then the system may collapse. It is the purpose of this paper to discuss certain aspects of the cardiac mechanism, the problem of coronary occlusive disease and its pathogenesis and particularly the value of current clinical electrocardiographic methods in detecting such disease.

Cardiac infarction is one of the most important causes of death and one of the most important complications of atherosclerosis. (1) Nearly 200,000 persons die each year from this cause in the

United States, approximately four times as many as die from diabetes and tuberculosis combined. (1)

It is planned that this paper will touch upon the historical development of the concept of coronary artery disease, its pathogenesis and pathology, and briefly, its therapy. The principle discussion will embrace the basis for normal patterns of myocardial excitation, the disruption of these patterns by certain forms of myocardial disease and the changes that occur as the heart attempts to restore its normal condition. The mechanisms of myocardial death in coronary occlusion will also be briefly noted.

A meticulously thorough history and a careful, complete physical examination are of great importance in studying the patient with heart disease. (2). The electrocardiogram, the roentgenograph and other laboratory data are of lesser importance but often are necessary for exact diagnosis. The ECG does not establish an etiologic diagnosis nor does it indicate the prognosis. The electrocardiogram does not discover the presence of valvular disease, the state of compensation of the heart or the state of cardiac reserve. It records only electrical events and may do this inaccurately. A patient may have no ECG evidence

of pathology and still have serious cardiac disease. (3, 4, 5) Conversely, if the ECG is abnormal, and extracardiac influences producing abnormalities can be eliminated, the patient has cardiac disease, regardless of all other clinical data. (5, 6)

The importance of a clinical diagnosis of myocardial infarction has been stressed since only a clinical diagnosis or a strong suspicion will stimulate the attending physician to obtain an electrocardiogram. The value of other laboratory and bedside tests available for diagnosis is recognized, but a discussion of their use is beyond the scope of this paper. (7, 8, 9) The problem of the clinically unrecognized or "silent" coronary (9, 10) is considered in the discussion of the illustrative cases presented.

It is commonly known that physical diagnosis is often unsatisfactory in the detection of coronary disease and too often the patient's history may be colored by his temperament and motives. (11) Furthermore, a language barrier can be insurmountable if a patient is in pain of such severity that he cannot give the attention needed to pass such an obstacle. It is in this area of heart disease that

the electrocardiogram is most commonly employed and it is this area which will be the subject of the bulk of this paper.

The electrocardiograph is no longer an exclusive diagnostic aid. The cardiologist has been joined by the surgeon, the obstetrician, the general physician and the pediatrician, all of whom employ this tool daily and interpret the records, not only of the patient but, in the case of the obstetrician, of the infant yet unborn. Electrocardiography achieves its greatest usefulness when supplementing sound clinical judgement. (12) The more information the physician interpreting electrocardiographic records has at his disposal, the more accurate and intelligent will be his final evaluation. The electrocardiogram is one of the most important aids in the diagnosis and in the localization of myocardial infarction. (13, 14) However, in about 25% of cases (13) it may fail to reveal evidence of existing infarction or it may give us an atypical picture.

Two precepts must be constantly borne in mind while examining electrocardiographic records. The first of these is that a "normal" record does not exclude cardiac disease, and the second is that

"abnormal" tracings might arise from a variety of causes, many of which are not of cardiac origin.

The question of the basis for clinical electrocardiography has been raised repeatedly (15) and cannot as yet be fully answered. One is struck, in reviewing the literature of electrocardiography, by the persistence of an empirical approach to interpretation and the construction of rather elaborate theory upon incompletely validated hypothesis. This criticism might perhaps be more justly leveled at other areas of medicine where scientific investigation is even less practicable but which none the less possess complex and intricate theory.

When one applies the test of practical worth to electrocardiography, one finds immediately that a great number of uses may be made of this device. Indeed the large number of factors which influence the pattern traced by the electrocardiograms operate to confuse the issue often, making it vastly important for the reader to fully comprehend all information available concerning the patient in question in order that the presence or absence of such possible influences (other than the basic pattern of excitation) may be evaluated.

To call the present methods of interpretation of electrocardiographic records empiric is not, by a considerable margin, strictly correct. A rational background of theory, expounded upon later in this discussion, permits the intelligent clinician to make reasonable judgements about the source of the impulse, its manner of spread, the presence of injury effects and the derivation of several diagnostic criteria. This, however, does not nullify the fact that in the final analysis, like other clinical data, the electrocardiogram is interpreted empirically. If he (the reader) lacks common sense, if he reads too much into the record, if he fails to correlate the electrocardiogram with other clinical evidence, if he uses the record to confirm the prejudices which he has reached before taking the record, then it is better that this test be omitted.

The electrocardiogram is most authoratative in deciphering the rhythm of the heart. Certain conduction disturbances are almost exclusively determined electrocardiographically. (16) The astute clinician can only make an educated guess as to their presence by use of the classical methods of physical diagnosis alone. (17)

The second contribution of the electrocardiogram is the recording of certain wave contours, the interpretations of which often allows a surprisingly exact diagnosis of cardiac pathology. It is in this area that empiricism is most strongly entrenched. Consideration of the wave forms as scalar representatives of the vectorial behavior of cardiac excitation and repolarization, enables the reader to more accurately envision the events which produced the record and relieve him of the necessity of laborious memorization of a multitude of patterns, each bearing an empirical diagnosis. (3)

The diagnosis of valvular disease cannot be made by solely electrocardiographic means, although correlation of certain valvular defects with their effects on the cardiac mechanism may be sufficient to arouse the suspicion of the reader as to the presence of such lesions. The ECG may be helpful also in estimating the condition of the myocardium in the presence of valvular disease. (4)

The conduction defects of certain congenital abnormalities are sufficiently characteristic to be of diagnostic importance (19), a matter of increasing importance in this period of ever-increasing worth

of surgical techniques in correction of such problems.

No information concerning the contractile power of the myocardium or its tone is provided by the electrocardiogram except insofar as that which experience has shown to be associated with electrocardiographic changes indicative of other conditions. (12)

The future of electrocardiography as a clinical tool is assured. The question of supplanting of the scalar cardiograph of today with spatial vector recorders cannot as yet be answered fully, but there is little doubt that sufficient information can be obtained from those devices commonly used to guarantee their use for many years to come. The convenience of these present recorders as compared with the complex equipment necessary for spatial vector-cardiography lends further weight to this view. For this reason, and others mentioned later, the principle portion of the remarks made on electrocardiographic utility and practice will refer to the present day scalar recorders.

The cause of myocardial infarction is prolonged (at least twenty minutes duration) disproportion between the nutritional requirements of the heart and the actual amount or quality of coronary blood flow. (20)

Roberts (21) proposes a listing of non-atheromatous causes of myocardial ischemia which includes as major groupings: (a) altered dynamics associated with aortic valvular disease; (b) anatomic coronary ostial narrowing; (c) coronary embolism; (d) congenital diseases of the coronary arteries; (e) manifestations of systemic disease; (f) increased cardiac load (as in rapid heart action); and (g) myocardial insufficiency (as in constrictive pericarditis).

Since coronary atherosclerosis and thrombosis are far and away the commonest causes of myocardial infarction, and since their development is so intimately connected with the electrocardiographic changes of this disease, a more elaborate mention of them will be undertaken than for the remainder of causes of infarction and its predecessor, ischemia.

An amassing body of data demonstrates the growing importance to medicine of the recognition that for man reactions to threats in the form of symbols, especially when sustained, may be more important than response to assaults. Many aspects of cardiovascular disease may be looked upon as functions of man's goals, his methods of achieving them, and the conflicts they engender. The finding of lowered blood lipids

during physical exercise and rising levels during stress endured without great physical exertion (22), the correlation of symptoms of cardiovascular disease with emotional and/or physical stress (23, 24), and studies of the incidence of coronary occlusion disease and race, social status, occupation, sex, age, diet, and habits such as tobacco (6, 25, 26, 27, 28, 29, 30, 31), and similar attempts at epidemiologic study of this problem have resulted only in confusion. This has been attributed to insufficient understanding of statistical methods and a lack of common values for measuring the factors known to contribute to such disease. (32) It is not merely academic to ask whether there are multiple causes for coronary artery disease. In the long journey from atheromatous flecking of a coronary artery to death from embarrassed myocardial blood supply several distinct causes may be operating and some may be more controllable than others.

HISTORY

The story of what is today the most important of all cardiac disorders, coronary artery disease and its consequences, may be said to begin in 1768 with Heberden's vivid clinical description of angina pectoris. (33) Prior to this milestone, work had been done on the problem of blood supply to the mycardium and the disease of these vessels but no correlation between the pain of angina and the condition of the coronary vessels was made. Actually Heberden mentions the heart but once and then as being normal, and he gave no indication that he associated the pain he so vividly described with coronary artery disease.

Galen is credited with naming the coronary vessels (34) and by the end of the sixteenth century the arteries had been portrayed in the De Fabrica of Vesalius (1543), but probably there was no clear notion of their function even up to the time of Harvey's De Motu Cordis (1628).

In spite of the investigation of coronary circulation (Vieussens, 1706, Thebesius, 1708) the Hippocratic notion that the heart was relatively immune to disease persisted. The conditions of this organ that attracted the attention of pathologists

were those associated with gross changes such as congenital malformations, pericarditis with its shaggy coat and fluid accumulations, and increased size of the heart. Disease of the coronaries was certainly present in many patients since physicians described precordial pain as well as dyspnea, cyanosis and altered pulse, but no mention of coronary disease was made at the bedside or at the dissecting table.

Changes now regarded as being due to primary disease of the coronary arteries were described by Lancisi (1654-1720). Lower (1631-1691) studied the coronaries, showing their anastomoses by experimentally injecting one artery from the other. Morgagni (De Sedibus et Causis Morborum, 1761) recorded cases with coronary changes and clinical symptoms like those of angina pectoris or coronary thrombosis. In general, however, these writer, even though recognizing the calcification of these arteries and the diffuse or partial aneurysmal dilitation of the heart, did not bring out clearly the function of the coronary arteries; did not realize that the changes in the size, contour and efficiency of the heart were due largely to the inability of the arteries to convey sufficient blood to the heart muscle. Also they had

no clear conception of the clinical picture produced by sudden or gradual interference with coronary blood flow.

Heberden in 1768 and again in 1782 drew his classical clinical picture of what he called angina pectoris, but even by 1782 had only a hazy view of the pathogenesis of this condition. Fothergill and Jenner regarded "ossified" and narrowed coronary arteries as the essential lesion in this condition. In 1809 Burns in his volume, Diseases of the Heart, described his experiment, that of the ligatured limb, designed to test the ischemic origin of anginal pain.

This theory has had a checkered career. It was promptly adopted or accepted in modified form by some, overlooked, rejected or vigorously combatted by others. (34) The controversy raged through many centers of medicine but oddly enough was not noted by Corvisart whose textbook on heart disease was the most popular of the day, not only in France but in Europe and the United States generally. Laennec also gave scant attention to angina pectoris or the coronary arteries. In Vienna there was the same striking absence of emphasis on this subject. Rokitansky despite his unparalleled necropsy experience, missed the opportunity of studying the coronary arteries. (35)

The leading argument explaining the changes seen in infarction was that the end result of coronary occlusion was fatty degeneration. The best known exponent of this theory was Sir Richard Quain (1816-1889). His writing and those of others of his school intrenched the concept of fatty degeneration so firmly in the traditions of medical teaching that it was difficult to supplant.

The earliest direct reference in the literature was Malmsten's report of a case of rupture of the left ventricle (1861). To Weigert (1880) is universally awarded the honor of being the expounder of the doctrine of cardiac infarction. Cohnheim (1881) established coronary disease as the cause of infarction, myofibrosis and aneurysm; parietal thrombus and heart rupture. He also established the secondary changes at the periphery of an infarct as the product of a nonpurulent inflammation having as its cause the disintegration of tissue elements. (35) The classical thesis of Odriozola (1888) and Rene Marie (1896) summed up and weighed the evidence of the masters and gave to clinical medicine a working basis for the study of myocardial disease, thus establishing the great principles enunciated by Weigert.

It seems strange that in spite of the writings of Weigert, Cohnhein, Huber (1882) and others showing the dominant part played by the coronary arteries in disease of the heart, no immediate widespread interest in the subject was aroused in clinicians.

One reason may have been that the views of Rokitansky and Virchow still were accepted as final. (34) These scholars in pathology while familiar with diseased coronary arteries and with softened areas or fibrous patches in the myocardium had expressed the opinion that these conditions were primarily inflammatory in nature.

A second reason may have been Cohnheim's indications that occlusion of the coronary arteries must result in sudden death. The subject, therefore, seemed to lack interest from the standpoint of the clinician.

A third reason was the overwhelming attention which physicians gave to physical diagnosis and valvular disease. The common view was that a heart in which auscultation and percussion could reveal nothing abnormal must be healthy.

A fourth reason was that the unity of coronary disease was hidden under the variety of captions applied

to manifestations of the disease - angina pectoris, cardiac neurosis, infarct of the myocardium, rupture of the heart, acute and chronic myocarditis, partial aneurysm - all these terms and more were used to discuss this disease.

At the time of these basic contributions the attention of the medical world was diverted not only from the coronary artery but in a measure from anatomic pathology by a series of discoveries that appeared in rapid succession and were revolutionary in character. Pasteur's paper on preventive vaccination appeared in 1880. In 1882 Koch announced the discovery of the tubercle bacillus and laid down his postulates. In 1886 Fitz read his classical paper on appendicitis. In 1896 Roentgen described the X-ray. No wonder that the coronary artery was relatively forgotten and that the medical journals were filled with discussions about antisepsis versus asepsis, the wonders of bacteriology and the revelations of the X-ray.

The clinical picture associated with coronary thrombosis was first clearly described by Herrick in 1912 (36) and by the 1920's the heart was again a subject of much interest. The contributions of Einthoven (1903) and Thomas Lewis (1911), the names of His,

Keith, Fleck, Gaskell; Roentgen diagnosis of cardiac conditions, these were topics of much discussion and interest. In the last two or three decades so much has been learned about the coronary arteries and their role in heart disease that this problem is now considered the single most important aspect of cardiology. Further historical notes are included in the ensuing discussion as they seem appropriate.

PATHOGENESIS OF MYOCARDIAL INFARCTION

An infarct, according to Dorland's dictionary (37), is "an area of coagulation necrosis in a tissue due to local anemia resulting from obstruction of circulation to the area." An infarct (1) is a necrotic focus which results when the blood supply to the part decreases below those limits which the tissue can tolerate. This decrease may be absolute, as in sudden occlusion of an artery with virtually no collateral branches, or relative, as in (a) occlusion of an artery with anastomotic branches distal to the point of occlusion; (b) suddenly increased requirements of blood by the tissues in the presence of vascular disease which prevents increased circulation; or, rarely, (c) marked hypotension. Infarction, therefore, is an effect of ischemia. Ischemia, however, is a relative term; depending upon the degree of ischemia, the effects may vary from practically nothing to necrosis. The duration of ischemia is also a factor, i.e. transient ischemia of cardiac muscle sufficient to produce pain clinically described as angina pectoris is often without significant permanent effect whereas more prolonged ischemia produces irreversible

degenerative changes.

The etiology and pathogenesis of infarction must be approached with three factors in mind: 1) the vascular-circulatory pattern of the tissue, 2) the mechanism responsible for ischemia, and 3) the blood supply required by the tissue.

The normal arterial circulation to the heart is supplied by modified vasa vasorum, i.e. by a right and a left coronary artery and their branches. The right coronary artery originates from the anterior aortic sinus at the base of the aorta and enters the atrio-ventricular groove to descend along the posterior longitudinal sulcus, in which it continues to the apex of the heart, where it anastomoses with the left coronary artery. (38) Along its course it gives off a small right ventricular artery to the anterior surface of the right ventricle; a large right marginal branch which descends along the right margin of the heart, sometimes as far as the apex; a posterior longitudinal along the posterior longitudinal sulcus to the ventricular wall. It sends twigs to the aorta, right atrium and to the fat adjacent to its course.

The left coronary artery emerges from the posterior aortic sinus between the base of the pulmonary artery and the margin of the left auricle. The artery first forks into two large branches and one small branch. The first sizable one descends in the interventricular groove as the interventricular artery (anterior descending branch of left coronary artery); the small middle one is the left anterior ventricular artery supplying the left ventricular wall in the region between the interventricular artery and the left marginal artery; the third branch circles around the left atrium under the left auricle as the circumflex artery. (38)

The latter gives off the left marginal artery which descends toward the apex. The circumflex terminates on the posterior wall of the left ventricle as the left posterior ventricular artery. Small branches supply the aortic wall as well as the fat at its base; along the course of the artery twigs also supply the atrium.

Venous blood of the heart is returned to the right atrium by the coronary sinus and its tributaries; by the accessory veins and thebesian vessels. The coronary sinus occupies the atrio-ventricular groove

on the left posterior side of the heart. It opens into the right atrium between the ostium of the inferior vena cava and the right atrio-ventricular valve. The valve of the coronary sinus, represented by a single fold, separates the sinus from the atrium. Opening into the sinus, beginning on the anterior surface, are the great cardiac veins which originate at the apex and ascend in the interventricular sulcus; a left marginal vein at the left side; a posterior vein of left ventricle on the diaphragmatic surface of the left ventricle; a middle cardiac vein in the posterior longitudinal groove. The oblique vein of Marshall opens near the left extremity of the sinus and the small cardiac vein lies between right atrium and ventricle. The vein of Marshall descends obliquely over the back of the atrium. (38)

Besides this drainage system into the right atrium, two or three small anterior cardiac veins ascend along the right ventricle and empty directly into the right atrium, while the smallest cardiac veins or veins of Thebesius, take origin in the heart wall and open into both atria as well as into both ventricles.

A well integrated description of the normal coronary circulation is that of Spalteholz (1924). (39)

His study showed a symmetrical distribution of right and left coronary arteries to be most common, while the right coronary artery was predominant in 17% of cases and the left coronary preponderant in 10% of cases. More recently Schlesinger (40) (1938) showed right coronary artery predominance in 48%, left coronary predominance in 18% and balanced circulation in 34% of his cases.

To the anatomist, an end artery is an artery which does not communicate with other arteries through anastomotic connections, thus its capillary bed receives blood from no other artery. To the physiologist, an end artery is an artery which alone supplies sufficient blood to an area to maintain its function and integrity; when this vessel is occluded the dependent area undergoes loss of function or necrosis because other arteries do not supply the given area sufficiently. (41) These definitions do not always coincide. (42)

The vascular-circulatory pattern is important in as much as the presence of adequate collateral circulation circumvents the damage which would otherwise follow occlusion of an area's principal blood supply (collateral circulation is interpreted to mean the

vascular pathway supplying an area in the reduction or absence of that area's principal supply). The effectiveness of collateral channels depends upon several factors, among which are: 1) the extent of the area requiring collateral supply, 2) the demand of that area for blood, 3) the time (suddenly or gradually) in which the need for collateral circulation arises, 4) the size and number of collateral pathways, 5) the general condition of the body as a whole, and 6) the ability of the body to provide new channels. (43)

The subject of coronary interarterial anastomoses has been studied since 1669 when Lower described connections between vessels of the heart. (44) Simple dissections of both human and animal coronary vessels has been supplemented by injections with various materials. Water, air, suet, wax, oils, dyes, turpentine, inks, starch, bacteria, Wood's metal, mercury, iron, bismuth and lead compounds, microscopic glass spheres, radio-active erythrocytes, celloidin, gelatin, latex, liquid nylon, water solutions of fluorescein, radio-opaque substances and other materials have been used. (45)

One of the most thorough studies of this problem is that of Zoll, Wessler and Schlesinger (1951), whose series of 1050 hearts was tabulated to show the

following findings. Only 9% of hearts in normal, non-anemic subjects had interarterial anastomoses whereas 39% of grossly normal hearts in anemic patients showed such connections. The incidence of anastomotic channels was 89 to 100% in cases of coronary artery occlusions, 11% to 63% with coronary artery narrowing, 73% with cor pulmonale, 28% with cardiac hypertrophy and 28% with valvular disease. The factor of relative cardiac anoxia that is present in all of the conditions appears to be a common underlying stimulus for the development of interarterial coronary anastomoses. (44)

Schlesinger (1940) observed myocardial infarct most frequently in those hearts with a dominant left coronary artery pattern of circulation, next in those with a predominant right coronary artery and least frequently in those hearts with balanced circulation. (45) Furthermore, in the left coronary predominant group the first infarct was most likely to be fatal, whereas multiple infarcts (healed and fresh) were most common in the right preponderant group.

Blumgart and his group (41) in studies on the pig, whose coronary vascular pattern corresponds more closely to the human situation than does the dog, found that if a major artery is ligated close to its origin,

a large infarct of the area supplied by the artery almost invariably develops. This corresponds in general with the usual consequences of a similar acute coronary occlusion in humans and suggests that functionally at least these vessels may act as end arteries even though anatomic anastomoses are present and establish a functioning collateral circulation. On the other hand, the acute experimental occlusion of a secondary branch or the acute occlusion of a major branch in its distal portion usually caused no infarct and no significant circulatory disturbances because under such circumstances the collateral circulation is capable of maintaining an adequate blood supply to the affected area of myocardium. Only complete sudden occlusion or acute narrowing to less than 13% of the original cross-section area of the right coronary artery at its midpoint or the left anterior descending artery near its origin was generally incompatible with survival; ventricular fibrillation or cardiac standstill usually occurs within twenty minutes. Collateral circulation in those surviving subjects appeared within two weeks after occlusion or narrowing.

With a rather elaborate technique Snow and his group (46) also were able to show that obstruction of

a main coronary artery almost inevitably leads to myocardial infarction. Coronary occlusion without infarction in their study was rare.

Many techniques to equate blood supply to the myocardium with the demand for nutrition by the heart have been contrived. The methods used can be roughly divided into those attempting to reduce the work load of the heart with an impaired blood supply and those means of increasing blood supply to the ischemic heart. Reduced activity, diet, medication to retard formation of atheromatous plaques and anticoagulant medication constitute the medical approach. (47) Surgical approaches such as abrasion or irritation of the epicardium (45), arteriolization of the coronary sinus (48), and grafting of other structures to the heart in an effort to stimulate production of collateral channels (49) have been attempted, but at present actual collateral channels subsequent to surgical approaches are not well proved and most reports of such techniques emphasize symptom relief. (45, 50, 51) Some workers, however, maintain some permanent protection against death result from surgical attacks on coronary artery disease. (52, 53) Other studies indicate merely a placebo effect. (54, 55)

The mechanisms responsible for ischemia fall into two principal categories (1): primarily functional and primarily mechanical. There are at least four possibilities to consider under functional causes: 1) arterial spasm; 2) marked hypotension, either from cardiac failure or from peripheral vascular failure (shock); 3) anemia or any other condition markedly reducing the oxygen saturation of hemoglobin, e.g. carbon monoxide poisoning; and 4) an effect from demands of the tissue requiring a relatively sudden increase in blood supply.

The question of vasospasm as a cause of infarction has not been fully answered. (56) No mention of spontaneous local or neurogenic "spasm" of coronary arteries was noted in the literature reviewed for this paper. The possibility of drug induced constriction (as with ergotamine) must be considered. (57)

The patient with hypertension (whose heart is apt to be greatly hypertrophied and whose coronary arteries are frequently narrowed by arteriosclerosis) when subject to a marked drop in blood pressure is likely to suffer severe cardiac ischemia with formation of many small foci of ischemic necrosis, so-called microinfarcts. (1) The myocardium receives an insufficient supply of blood during many of the arrhythmias,

particularly if hypotension is present. (63)

Fatty change in the heart may follow severe anemia or other conditions involving the blood to cause hypoxia. (2) Sudden increase in requirement of blood because of increased demands for functions may produce (in absence of adequate coronary reserve) sufficient ischemia for infarction to develop. (24) This may conceivably follow administration of epinephrine to a patient with coronary insufficiency.

Sudden mechanical occlusion of an artery is by far the most common cause of infarction because this is one of the most effective ways to suddenly deprive a tissue of most of its blood supply. Most often it is accomplished by thrombosis or embolism. The possibility of venous obstruction as a cause of myocardial infarction is remote. (1)

Platz (58) estimated that from 90 to 95% of myocardial infarcts result from coronary sclerosis. In Yater's series (59) approximately one-half were associated with thrombolic occlusion alone, one-fourth with sclerotic occlusion alone, and one-fourth with both sclerotic and thrombolic occlusion. In most cases, all three main coronary vessels were involved by atherosclerosis. A second study by Yater and his group (60)

showed additionally that coronary artery carries a more serious prognosis for men under 40 than for men aged 40 and over.

Hamman's observation (61) that the diagnosis of coronary embolism was first made at Johns Hopkins in 1931 and ten times in the succeeding nine years illustrates the recent advent of this disease as a clinical entity despite the many descriptions of the symptoms complex produced by coronary occlusion alluded to in the historical note included in this paper. Hamman postulated that one or two percent of coronary occlusions are due to embolus. The rarity of embolic occlusion of the coronary arteries together with the multiplicity of conditions associated with it make clinical diagnosis difficult. The diagnosis may be suggested when death occurs instantaneously. (4, 62) Most commonly this catastrophe is associated with subacute bacterial endocarditis. Bland blood thrombi from various locations, (mural thrombi, thrombi or aortic atherosclerotic plaques, thrombi in peripheral veins by paradoxical embolism mechanism, etc.) and, rarely, solid tumor emboli have also been implicated. Fat and air emboli commonly are thought to produce death from obstruction of pulmonary and cerebral, rather than coronary, vessels.

The recognition of a peculiar distribution and form of myocardial necrosis limited in great part to the subendocardial musculature and papillary muscles of the left ventricle, in the absence of recent coronary artery occlusion, has stimulated the survey of the anatomic alteration and the mechanism responsible for their production. (64) Although considerable investigation of the conditions necessary for production of this lesion (increased nutritional demand of papillary muscles, oxygen deprivation of endocardial layers by systolic pressure gradient interference with coronary flow, etc.) has been done, the reason for its localization to the layers described is still a subject for speculation. A variety of factors appear to have precipitated this state, including tachycardia, acute heart failure, acute hemorrhage, pulmonary embolism, dissecting aortic aneurysm and severe infection. (65) An interesting recent report (66) adds reactions to tetanus antitoxin to the list of causes.

The two most common causes of coronary artery occlusion will be considered in greater detail.

The first of these, atherosclerosis, has (according to Morgan) until quite recently been regarded in the same frame of reference as the phenomena of

aging, the implicit assumption being made that just as all living creatures pass inevitably from a period of growth and maturation into one of senility and decay, so too the vascular channels harden and wear out. (67, 68) Hence the degenerative changes in blood vessels came to be looked upon as the natural and inexorable sequelae of life, the price that human tissue paid for prolonged survival. This acceptance of arteriosclerosis as a natural process was for many years responsible for retarding fruitful investigation into its etiology and pathogenesis. It was not until the third and fourth decades of the present century that it became increasingly clear, from clinical, morphological and experimental observations that arteriosclerosis constituted more than a single morbid process and, furthermore, that its most serious manifestations were not essential concomitants of aging, but represented rather an acquired abnormality. This change in concept was an important one for it came at a time when the infectious diseases had in large part been mastered and when diseases of the heart and blood vessels were becoming foremost among the afflictions of mankind.

The imperfections of nomenclature have often proved a source of confusion in medicine, and to this

the term arteriosclerosis is no exception. Coined by Lobstein (69) in 1833, it is a generic term applied to a group of vascular diseases characterized morphologically by hardening of the vessel wall, and including such heterogenous conditions as atherosclerosis, medial sclerosis, arteriolosclerosis and the physiologic changes (insofar as is known) of the normal aging process. Of these, atherosclerosis alone is a primary concern in the problem of coronary artery occlusion.

In the absence of more precise knowledge of its etiology and pathogenesis, atherosclerosis is for the present best described in morphological terms; its distinctive and fundamental feature being the presence of stainable lipid within the lesions. Lipid accumulations in walls of arteries have been described in children and, much more commonly, in adults. (22, 70) The pathogenesis is thought to consist of an interaction of an area of injury in an artery (hypertension, trauma, etc.) with lipids, particularly cholesterol, derived from the plasma to yield an invasion of the intima and later the media of the vessel by lipid deposits. It has been demonstrated (22) that emotional stress not only is capable of elevating blood pressure but can produce a rise in serum cholesterol levels and thus

expedite formation of atheromatous deposits. The high fat diet of Western man has been accused of contributing to the rising incidence of this disease. (71)

The result of repeated or constant deposition of lipids in the vessel walls is an accumulation - first multifocal, then confluent - of sufficient fatty material to impinge upon and often eventually occlude the lumen of the involved vessel. This disease, which primarily affects the nutrient vessels of the heart, brain and kidneys, leads to sufficient deprivation of blood supply to produce functional alterations and, all too commonly, death.

As the disease progresses, the lipid-containing foam cells in the vessel wall undergo necrosis and discharge their contents to convert the central portion of the lesion into a soft, pultaceous mass - the atheroma from which the entire process derives its name. In time, secondary changes become manifest, prominent among which are thickening of the overlying endothelium, disruption of the elastica with invasion of the media, fibrosis, hyalinization and calcification. The continued growth of the lesion leads to diminution of the caliber of the vessel and slowly throttles the flow of blood. Not infrequently, the flow of blood in

atherosclerotic vessels, particularly coronary vessels, is halted more abruptly by thrombosis or hemorrhage into an atheromatous area. This complication is thought by many to form the commonest cause of myocardial infarctions. (72)

The great expectations fostered in the last decade by the biochemical approach to the problems of atherosclerosis and coronary disease have not so far been fulfilled. A recent review (67) summarized the current course of investigations of this problem by stating that not one conclusion reached by workers in this field had escaped serious challenge by other students of repute in the same areas. Even the increased incidence of coronary disease revealed by vital statistics has been called largely artificial. (73) Most studies have focused attention on the concentrations of serum cholesterol, serum lipid or serum lipoprotein, without proper emphasis on the focus of the problem, which is atheroma and infarction. (74)

The observations of Morgan (67), Duguid (75) and others led these workers to conclude that coronary occlusion is the result of thrombosis and not of lipid infiltration alone; that coronary "atheroma" and "coronary disease" are separate entities and that "atheroma"

is not the only factor in coronary thrombosis. The "thrombogenic" theory of Morgan (67) and the concept of gradual accumulation of lipid deposits are mutually exclusive since Morgan postulates that coronary disease is episodic and characterized by sudden occlusions which occasionally shrink rapidly and become molded against the vessel wall in the form of a crescent, thus re-establishing circulation to a greater or lesser degree and explaining the presence of healed infarcts without associated complete occlusion of the nutrient vessel. He further suggests that the bulk of cholesterol in the atheromatous plaques is derived from red cell breakdown following hemorrhage into the plaque. He finally proposes that anticoagulant therapy, while reducing thrombo-embolic sequelae of infarctions, increases the tendency to intimal hemorrhage, which is a subsidiary cause of occlusion.

Under conditions of normal arterial oxygen content the oxygen requirement of the heart, which is contingent on the degree of effect, is adjusted by the coronary blood flow rather than by a change in the percentage of oxygen extraction. (76, 77, 78) Despite differences in the manner of increasing cardiac performance, the a-v oxygen difference does not vary more

than 1-2 vol.% from the mean value. Thus the relationship between oxygen availability and cardiac oxygen consumption is a constant one since the percentage of oxygen extraction does not change.

Myocardium, unlike skeletal muscle, demands oxygen pari passu with activity. When the supply of oxygen is limited the subsequent protection of myocardial integrity depends on the response and capacity of the coronary vasculation to augment blood flow and maintain normal oxygen availability. Another possibility would be an increase in oxygen extraction from the available supply. This possibility was eliminated by Feinberg et al. (78)

The metabolism of the myocardium is almost entirely aerobic under normal conditions, and a significant oxygen debt probably does not develop. (79, 80, 81)

The primary factor in the determination of myocardial energy requirements measured in terms of its oxygen utilization appears to be the tension produced by the contracting heart muscle. (82, 83) The coronary blood flow is directly related to the myocardial oxygen uptake. Thus, any increase in coronary blood flow is produced by an increased demand of the myocardium for oxygen.

The myocardium has the ability to utilize several types of foodstuff for its metabolism. (79, 84) In general the substance selected as the major energy source is the metabolite available in the greatest quantity at the given time, however there is a marked preference for glucose. When carbohydrates are not readily obtainable, fatty acids, and in particular the unesterified fatty acids, become the major source of oxidative energy. (85) Amino acids and ketones can also become food for the myocardium when needed. The deprivation of oxygen resulting from ischemia, however, does not allow utilization of this since all metabolic pathways involved are oxidative in nature.

When myocardial ischemia supervenes there are metabolic alterations involving all substances, particularly a decreased oxygen and lactate utilization. Apparently active oxidation is interfered with, and no compensating change in coronary blood flow is possible. The enzyme system involved in the utilization of oxygen and lactate appears most sensitive to anoxia and is probably damaged. (84, 86, 87)

The chief consequences of coronary artery occlusion is infarct. White (88) lists the following factors which determine the occurrence of this hazard: 1) size

of occluded vessel, 2) site of occlusion, 3) speed of occlusion, 4) condition of other major coronary arteries, 5) anatomic patterns of coronary vessels, 6) the effect of cardiac hypertrophy, 7) the extent of congenital and/or acquired anastomotic or collateral coronary circulation and possibly also other blood channels including the Thebesian circulation and extracardiac blood vessels in the pericardial attachments.

The immediate effect with massive infarct is cardiac arrest and sudden death. If the infarct is not immediately fatal, forward failure of varying degree occurs. (1) Failure of the deep bulbospiral muscle produces a marked drop in blood pressure and is probably the basis for the shock which so often follows infarction and which is responsible for a large proportion of the non-immediate deaths which occur within the first forty-eight hours. (1, 42, 89)

Another explanation for the decrease or cessation of cardiac output following infarction is that of Murray (90) who reports creating a "paradoxical systole" in which the infarcted area dilated during mechanical systole thus reducing outflow by absorbing a portion of the blood which is normally expelled into the aorta. He demonstrated this phenomenon in dogs subjected to ligation of coronary arteries. As a result of his

observation, he advised surgical resection of the infarcted area to eliminate this "paradoxical systole" and reported 80% survisal in animals undergoing such treatment. This paradoxical motion may contribute to the S-T vector changes of acute infarction. (3)

Aside from heart failure itself the most serious consequence of cardiac infarction is embolism. Any infarct of the heart which extends to involve or closely approach the endocardium leads to mural thrombosis and this is a likely source of one or more thrombo-emboli. Of patients with cardiac infarcts, approximately one-fourth develop thrombo-embolic complications. With treatment by anticoagulants the incidence of significant thrombo-embolic complications drops to approximately ten percent. It is important to realize that here again much depends upon the pattern of coronary vessel distribution. (It is not surprising that thrombo-embolic complications in the lungs may complicate a cardiac infarct which appears electrocardiographically to be localized principally to the anterior aspect of the left ventricle. (1)

Mallory and his group (91) described the changes in infarction in a series of cases in which the onset of clinical findings allowed determination of the age of the infarct. Their findings may be summarized thus:

1. Necrosis of muscle, connective tissue and smaller blood vessels. Necrosis does not become evident for five or six hours; the muscle fibers then become hyaline and take a deeper acid stain, while the striations become less evident, the nuclei undergo pyknosis, karyorrhexis or karyolysis. A layer of intact muscle, 0.3 to 0.5 mm. thick, usually persists beneath the endocardium, the nourishment for these fibers apparently being provided directly by the blood in the cavity of the heart and in the Thebesian veins.

2. Hemorrhage is usually focal rather than diffuse and extravasations are relatively rare. The venules and capillaries are hyperemic. Hemolysis of erythrocytes results in deposition of hemosiderin which is phagocytized by macrophages. The infarction has features of both hemorrhagic and anemic types.

3. Fat varies in amount depending on the suddenness of infarction and previous sufficiency of circulation. Most of the fat is found at the periphery of the infarct. The fat is removed by the macrophages at the same time as the necrotic muscle. The fat may represent dead or dying muscle or an accumulation of leukocytes.

4. Infiltration with polymorphonuclear leukocytes begins at about five hours, starting at the

edges of the lesion and spreading centrally. It is present in the interstitial tissue and about the blood vessels and gradually extends into the necrotic tissue. At 24 hours, the infiltration of polymorphonuclears is slight, with beginning degenerations of leukocytes; at five days, many of the polymorphonuclears are necrotic; and thereafter they gradually disappear. Eosinophilic polymorphonuclears are also seen between the fourth and eighteenth days.

5. Ingrowth of blood vessels and connective tissues begins on about the fourth day when new capillaries grow into the infarcted area, starting peripherally. Fibroblasts accompany the blood vessels. The ingrowth is relatively greater on the epicardial than on the endocardial side. If the infarct is large, the vascularization may not reach the center.

6. Simultaneously with the ingrowth of new capillaries and fibroblasts, macrophages invade and phagocytize the necrotic cells. Occasionally giant cells may appear. The fragments of muscle dissolve and disappear but their lipoprotein remains within the macrophages which become pigmented. Some macrophages also contain hemosiderin which is produced from the breakdown of the red blood cells in areas of hemorrhage. After about ten days, one millimeter of necrotic

peripheral muscle has been removed and after six weeks active absorption of necrotic muscle fibers may still be present. At two months, necrotic muscle fibers have generally been completely removed. After one year practically all pigmented macrophages have disappeared.

7. Lymphocytes and plasma cells appear as soon as absorption of muscle starts, are fairly prominent during the third week and disappear about the same time as the pigmented macrophages. Occasionally mononuclear cells persist for many months.

8. Collagen produced by the fibroblasts appears first at twelve days, is prominent at three weeks and maximal at two to three months. The amount of collagen provides a good indication of the age of the infarct. At six weeks the scar becomes contracted. Adjacent to old infarcts the muscular fibers are often hypertrophic and their nuclei hyperchromatic.

9. Pericarditis which is fibrinous in type appears within 24 hours. Organization of the exudate begins at eight days or earlier and is complete at four weeks. The pericardial reaction also provides a basis for judging age of the infarct.

10. Endocardial thrombosis begins as early as five days but may occur much later. It is thought by some (92) to be the result, not of the infarct, but of

secondary dilatation of the infarcted wall. Its organization may be present on the sixteenth day and begins on the ninth day. Organization of the thrombosis, however, is not a reliable guide in estimating the age of the infarct.

Mallory and his associates (91) pointed out that, from the microscopic picture the age of an infarct may be judged well during the first three weeks; that small infarcts heal more rapidly than large ones; that subendocardial infarcts heal less rapidly than those in the center of the myocardium or beneath the epicardium; and that the rate of healing depends on the competency of the remaining circulation and, therefore, on the degree of coronary arteriosclerosis, and on the amount of heart failure and anemia. The clinical correlation of pathologic studies has been presented by Jennings and Wartman. (87)

GENESIS OF ELECTRICAL ACTIVITY OF THE HEART

According to the membrane theory (93) living, resting cells, including myocardial cells, are regarded as being surrounded by a semi-permeable membrane lined by a series of electrical doublets or dipoles with the negative charges on the inner and the positive charges on the outer surface. By pairing a microelectrode inserted into a cardiac cell with an electrode on the surface of the cell, a large transmembrane potential difference has been demonstrated; the inside being about 85 millivolts negative with respect to the outer surface. (94)

When the membrane is electrically "intact", its entire surface is surrounded by doublets and it is said to be polarized. This orientation of charges is probably due to movement of positively and negatively charged ions, and is at least partially explained by Bernstein's membrane hypothesis, elaborated in 1913. (95) According to this hypothesis each element of a resting muscle is surrounded by a membrane permeable to the positive ion or cation, but impermeable to the negative ion or anion, of some dissociated electrolyte within the muscle substance. As a result of the semipermeable character of the membrane, the cations pass through it freely, but

the anions are held back; consequently, a condition of equilibrium is established in which the electrostatic force between the positive charges held by the cations on the outer surface of the membrane and the negative charges held by the anions on its inner surface, a force which tends to prevent further outward migration of cations, is balanced by the diffusion pressure or osmotic which results from a difference in the concentration of these ions on the two sides of the membrane. Under these circumstances, then there is a layer of anions carrying negative charges lining the inner face of the membrane and a corresponding layer of cations carrying positive charges upon the outer surface of the membrane. A membrane which is the seat of such a double layer has been referred to by physiologists as polarized.

The two cations which seem to be most concerned with this difference of potential are sodium and potassium. (95) The concentration of potassium inside the cell is about fifty times greater than in the interstated space outside the cell; that of sodium, on the other hand, is much greater on the outside of the cell than on the inside. (96) There are, therefore, diffusion pressures set up which would tend to cause a

migration of sodium ions in the opposite direction. such migration occurs, however, because this tendency of the respective ions is counterbalanced by the electrostatic forces between the positively charged ions on the outside of the cell and the negatively charged ones inside the cell.

Once a cell has been stimulated a flow of ions does occur. Ions move not only because of a concentration gradient (consequent upon their varying concentrations on the two sides of the membrane) but also under the influence of an electrical field and a frictional resistance proportioned to the velocity of the ions in the membrane. (97)

When a resting, excitable cell is stimulated, profound changes take place. In the case of the normal heart, these stimuli arise in the sinoauricular node, then spread through the atria and the specialized conduction system of the ventricles in a well known manner. (98) Upon arrival of the stimuli at the muscle cell, its membrane becomes permeable to both anion and cation. The resistance of the membrane decreases about fifty-fold! (99) As a result, the conductance (the reciprocal of resistance) increases up to 200 times that of its resting value, (96) with simultaneous decrease in the electromotive force across the membrane.

This change in permeability of the membrane permits a free flow of ions through the membrane. When the membrane potential is thus suddenly reduced (depolarization), the initial pulse of current through the capacity of the membrane is followed by sodium and potassium currents, moving down their own electrochemical gradients. (97) The first current that flows consists of sodium ions. Since, when the cell is resting, the concentration of these ions is greater outside than inside the cell, the flow of current is from the exterior to the interior of the cell, thus depolarizing the membrane still further, until the membrane potential reverses its sign and approaches a value at which sodium ions are in equilibrium. Potassium currents start flowing shortly after the beginning of sodium mobilization. Since the concentration of potassium is greater inside the cell than outside, the flow of this current is directed from within outward. When it exceeds the sodium current, it starts the repolarization of the membrane.

The net effect of the migration of ions just described is that the membrane potential rapidly falls to zero (depolarization) and then reverses itself so that the inside of the cell becomes positive with respect to the outside (reversal of polarization or

"overshoot". (96) This reversal of potential is a very fleeting phenomenon, for it is rapidly supplanted by the changes that take place during recovery phase. That the reversal actually occurs, however, has been proved by experiments with lower forms of life. (99, 100)

Following very quickly upon the process of activation just described, recovery sets in. Current now flows between muscle regions just polarized and those still depolarized as a result of activation. The membrane is thus finally repolarized completely and regains its selective permeability; and the double ionic layer characteristic of the resting state - positive charges on the outside and negative charges on the inside - is re-established.

In a small percentage of these cases, Woodbury and associates (100) noticed an "overshoot" of reversed polarization mentioned above. In these instances, the membrane potential early in diastole was greater even than that of the controls measured during rest. These authors called this process "hyperpolarization."

The mechanisms of ion transport are not well understood. Grant (3) simply refers to "cellular metabolism" which "proceeds to repair the semipermeability of the membranes." Although the fluxes of sodium and potassium have been well documented (95, 97, 101, 102),

the nature of serial changes in membrane permeability which regulate the fluxes of these two ion species is unknown. (103) Some workers suggest that acetylcholine is implicated in causing alterations in the molecular structure of the membrane during activity. (104) Others indicate that the amount of heat generated is too small to suggest an origin other than that due to movements of ions through the membrane. (95) Calcium ion is believed to be active in regulating membrane permeability, (105) although it plays no direct role in generating the transmembrane potential. It appears likely that in the future advances of electrocardiography will be made by better understanding of these mechanisms and the physiochemical forces that control them.

The changes in myocardial tissue which produce polarization and repolarization do not occur instantaneously. Excitation (depolarization) proceeds in a wavelike manner from the point of stimulation down the muscle fiber to its distal end. The heart muscle is a syncytium and excitation probably occurs in a rather complex manner. It is convenient (and conventional) to consider single muscle fibers when descending the electric field of activity and, by a rather wide step, generalize about the behavior of the heart as a whole

during depolarization and repolarization. A further basic premise necessary for interpretation of activity by electrocardiographic means is that the body acts as a volume conductor.

BASICS OF ELECTROCARDIOGRAPHIC RECORDING

By imagining a cardiac fiber immersed in a conducting medium, it becomes possible to analyze the events which occur as the activation wave spreads.

Under these conditions an electric current is established which flows through the medium, the direction of the current being from the unactivated muscular portion to those which have already been activated. This means that there is a difference in potential between the activated portions and those not yet activated, the former being negative with respect to the latter. There are likewise differences of potential in the surrounding medium; without them current could not exist.

The point at which the greatest amount of current flows out from the muscular tissue into the conducting medium has the greatest positive potential and may be called the "source" or place of greatest positivity of the medium. It corresponds to the front of the activation wave. The point at which the greatest amount of current flows from the conducting medium into the muscular tissue is that with the greatest negative potential; this point may be called the "sink." It corresponds to the tail of the activation wave. (96, 106, 107)

Thus is created in the medium, but intimately related to the muscular fiber, a dipole, which in turn sets up an electric field throughout the medium which surrounds the muscle. Moreover, this dipole in effect moves through the medium as the activation process proceeds from one end of the fiber to the other.

If the medium is strictly homogenous, a number of equipotential surfaces are formed around the two charges of the successive dipoles. The amount of current flow reaches its maximum at the crest of the activation wave. The potential produced by the dipole approaches zero at points distant from the tissues, regardless, to a certain extent, of the actual orientation of the dipole. (96, 107)

The potential (V) of a point in the conducting medium is given by the formula: $Vp = \frac{\pm Q}{r_1} \pm \frac{-Q}{r_2}$ where $\pm Q$ and $-Q$ represent strength of the source and sink of the dipole, respectively; and r_1 and r_2 are the respective distances from $\pm Q$ and $-Q$ to the point p. (108)

At points distant from the dipole, as noted above, the potential approaches zero; this is readily evident from the above formula, for at such points r_1 and r_2 are of great magnitude and the voltage V is therefore small or even negligible. If r_1 is smaller

than r_2 the potential at p is positive; if it is the voltage at p is negative.

It was on these principles that the earliest precordial electrocardiogram depended. One electrode was attached to the leg, and being relatively far away from the heart, was considered as being zero potential. The other electrode was then placed at various points on the chest wall, close to the heart. The first was called "indifferent", the latter the "exploring" electrode. Further refinement of the method noted above provided the modern unipolar lead recording system. (109)

For the sake of clear thinking, it is important to distinguish between the source of the electrical field of the heart and the field itself. The source of the field consists of all the polarized surfaces which separate activated from resting muscle. The only circumstances under which an exploring electrode of a direct lead could be considered as being in intimate contact with the source is that instant at which the activation wave arrives immediately subjacent to the electrode; this is the instant when the intrinsic deflection is inscribed and it is transitory indeed. At all other times the electrical activity which the electrode is recording is occurring at some distance, near or far, from the electrode, even though the electrode is placed

directly on the heart. The greatest part of the curve, therefore, consists of a record of changes in the electrical field, that is it deals with extrinsic phenomena. Except for the polarized boundaries corresponding to the head of the activation wave, all the rest of the tissues of the body, including the parts of the heart just activated and those not yet activated, serve as a conducting medium; even the blood flowing through the chambers of the heart comprises a part of this medium. (96)

Of necessity, the recording of an electrocardiogram in man involves placing the electrodes far from the heart, over tissues which fortunately form part of the volume conducting medium surrounding this organ. Under such circumstances it is apparent that the potential variations which are being recorded are those of the electrical field of the heart rather than the potential differences at the polarized surfaces themselves. The active potential of the heart is not, contrary to writings of some workers, registered by the electrocardiogram. (96) The field is a reflection of activity taking place at the above-mentioned polarized surfaces and the existence of the field is the basis for all of clinical electrocardiography. (110)

Consideration of the events in depolarization and repolarization makes it clear that a cell in the resting (polarized) or in the excited (depolarized) state produces no outward electrical manifestation. Consequently, all of the normal electrical manifestations of the heartbeat occur while the heart's cells are passing from the resting into the excited state, and again while the cells are in the process of passing back from the excited into the resting state.

The development of electrocardiography has progressed through two major phases. Willem Einthoven (111) and Sir Thomas Lewis (112) were most notable in the earlier period (1905-1925) in which the method of recording bipolar leads and the major diagnostic features of the arrhythmias were set forth. Frank N. Wilson (113) pioneered the developments in the thirty years that followed. This work centered about the suitable applications of the laws that define the flow of currents in volume conductors, an extensive interpretation of the normal and abnormal QRS complex in the bipolar, semidirect and direct leads, the first proper interpretation of the potential distribution that is produced by the field of injury, and the integrative method of analysis of the accession and regression processes. (106)

The mathematical exposition of electrographic theory has been in large part the work of Robert Bayley. (106, 107)

This paper will concern itself almost entirely with the vector method of electrocardiographic interpretation. The understanding of, and practice with, the basic tools of this approach eliminate the hazardous and dubious task of pattern memorization of the multivaried wave forms that are displayed by modern electrocardiographic leads. With this knowledge deflections that are the least conspicuous may often be assigned a proper interpretation of first-order importance. Contrariwise, certain obvious pattern changes are not apt to receive empirical exaggeration in the light of coincidental clinical events.

The meaningfulness of the vector concept depends on the view first proposed by Waller (114) that the heart is an electrical source analogous to a dipole. This dipole is considered to be the resultant of all the electrical forces created by the ventricles and is placed in the center of the heart mass.

Einthoven (111) conceived of the human torso as a sphere at the center of which was the heart's electrical activity. The right shoulder, left shoulder and left hip (or pubis) - considering the limbs as mere

continuations of the lead wires from the galvanometer in the recording device - were regarded as forming the apices of an equilateral triangle and the points were further regarded as being on the surface of the body "sphere." The plane of the triangle was assumed to be parallel to the frontal plane and to contain the dipole at its center.

The Einthoven triangle hypothesis (115) also assumes that the tissues surrounding form a uniform volume conductor and therefore conduct the electrical impulse uniformly to the body surface, and further that the site of the limit electrodes represented by the apices of the Einthoven triangle are relatively distant from the heart and each other, the heart being represented as a point source of electromotive forces, denoted by the center of the equilateral triangle.

None of these assumptions is exactly correct since the heart is somewhat eccentrically placed in the torso (115), the triangle formed is not equilateral, the heart is not equidistant from the apices, the tissues are not uniform with respect to their conductivity (18, 117, 118) and the size of the heart is relatively large compared to the distance of the electrode from the heart. (4) However, the assumption approximates the facts sufficiently to have made the Einthoven hypothesis extremely useful in

understanding the findings in the electrocardiogram of the human heart. (118) The Einthoven hypothesis is the basis also for the concept of the mean electrical axis and determination of the manifest electromotive force of the heart; concepts which will be further developed in the discussion of vectorcardiography later in this paper.

Electrocardiographers have agreed (117) that in clinical practice a standard set of recording be taken and labeled in a conventional manner. The standard limb leads are bipole leads. Lead I is taken between electrodes placed on the right and left forearms; Lead II is between the right forearm and left leg; Lead III is between the left forearm and left leg. The polarity of the electrocardiogram is so arranged that an upright wave is recorded when the left arm electrode is positive relative to the right arm electrode; and upright wave appears in Lead II when the left leg electrode is positive relative to that on the right arm; an upright wave occurs in Lead III when the left leg electrode is positive relative to that of the left arm.

Since the standard leads are bipolar they reveal differences of potential at two sites but do not actually disclose the potential at any single extremity. The lead potential differences in microvolts at any instant is as

follows: Lead I = left arm minus right arm; Lead II = left leg minus right arm; Lead III = left leg minus left arm.

If electrocardiograms were taken simultaneously with all three standard limb leads, at any given instant the potential in Lead II is equal to the sum of the potentials of Leads I and III. This is Einthoven's Law. If, as is commonly done in clinical practice, the leads are recorded in succession, this relationship is only approximately correct but it is sufficiently close to allow the method to be used and thus greatly simplify the equipment necessary for clinical electrocardiography.

Goldberger (120) modified the unipolar limb leads as developed by Wilson in two respects. Wilson's original method, alluded to above, employed a central terminal (121) which was thought to represent eventually zero potential and which was attained by attaching it to each of the three extremity leads and interposing a resistance of 5000 ohms between each of these limbs and the central terminal, which was connected to the negative pole of the electrocardiographic galvanometer. The positive pole was connected to the exploring electrode through which positive potentials were recorded as upright waves. The concept upon which Wilson's work was based, that is, the approximate validity of Einthoven's law, has been

criticized (122) and Goldberger's modification has supplanted the unipolar leads as suggested by Wilson. Goldberger removed the 5000 ohm resistance and detached the limb under study, with electrode, from the central terminal and gained potential about 50% greater than actually present at the limb under study as it had been obtained with Wilson's method. The Goldberger leads are, therefore, termed augmented and symbolized by a for augmented, V for unipolar and L (left arm), R (right arm), or F (foot) for the limb being explored; aVL, aVF and aVR are now considered to be standard records in clinical electrocardiography. (4)

The chest leads in clinical practice at present are unipolar and labeled for the position on the chest wall occupied by the exploring lead: V_1 from the 4th ICS immediately to the right of the sternum; V_2 from 4th immediately to the left of the sternum; V_3 midway between $V_2$and V_4; V_4 5th ICS in left MCL; V_5 left anterior axillary line at horizontal level of V_4; V_6 left midaxillary line at same horizontal level as V_4 and V_5.

These make up the usual clinically employed leads. Additional leads on the right side of the chest (4), in the esophagus (123), intrabronchial (124) and intracardiac leads (126) have been employed. Only the right chest leads are commonly used clinically. (4). A

discussion of these leads is beyond the scope of this paper.

The electrocardiogram is composed of a series of waves designated in succession by the letters P, Q, R, S, T, and U. (119) The horizontal portions of the record are called segments and are designated by the letters of the preceding and following waves. The recording paper is marked in vertical time lines and the paper is fed past the recording stylus at such a rate that the interval between two fine vertical lines represents 0.04 seconds. For the convenience of the interpreter of the record, each fifth vertical line is darker and marks off 0.2 second. The distance or time interval between two waves is measured from the beginning of one wave (the point of departure from the horizontal segment or isoelectric line) to the beginning of the next. Horizontal lines parallel to the base (isoelectric) line are one mm. apart and the recorder is adjusted so that an excursion of ten millimeters is seen when one millivolt is added to the recording circuit. Again for convenience every fifth horizontal line is broader and the distance between two such lines is 0.5 millivolt.

The P wave represents the spread of the depolarization from the sinoatrial node along the atrial wall to the atrioventricular node. Repolarization of the atria

is represented by an atrial T wave (Tp or Ta) following the P wave and opposite in direction to the P wave. (125) The atrial T wave is usually invisible in conventional electrocardiograms either because of low amplitude or because it is concealed within the QRS complex. It may occur after the R wave and cause a slight depression of the S-T segment. (4)

The P-Q or P-R interval is measured from the beginning of the P wave to the Q wave or the beginning the R wave if no Q wave is present. The P-Q segment (from the end of P to the onset of Q) represents the delay in transmission of the impulse from atria to ventricles in the atrioventricular bundle and the bundle of His. The atrial T wave is usually hidden in this segment but may be visible if the P-R interval is prolonged.

The QRS complex (initial ventricular deflection) represents the depolarization of the ventricle. The Q wave is the first negative deflection (below the baseline) and the R wave is the first positive deflection. A downward deflection following the R wave is called an S wave. Second positive or negative deflections are called R^1 and S^1 respectively. If the entire complex consists of a single downward deflection, it is termed a QS wave. The interval from the onset of the QRS complex to the peak of the R wave is termed the intrinsicoid deflection.

The RS-T segment (R-T or S-T) is measured from the end of the QRS complex to the onset of the T wave and represents a state of unchanging polarization between the end of depolarization and the beginning of repolarization, or a stage at which terminal depolarization occurs simultaneously with, and is neutralized by, commencing repolarization. (4)

The T wave represents ventricular repolarization and occurs during the latter part of systole. The T wave is in the same direction as the major QRS deflection except in certain conditions of organic disease or transient physiologic disturbances. (4) This is thought to be due to repolarization beginning in the sub-epicardial region and continuing in an opposite direction from that followed by depolarizing events. (127)

The Q-T interval represents the duration of ventricular electrical systole, including depolarization and repolarization. It is measured from the beginning of the QRS complex to the end of the T wave, commonly in the lead with the most distinct T wave. Accurate measurement is often impossible when the T wave is low, when a well developed U wave is present or when P and T are superimposed. (128)

The U wave is a low, broad wave which is present in a majority of subjects (129) and whose origins are

unknown. It has been attributed to the mechanical effect of ventricular distention during the early phase of rapid filling and also as a manifestation of after-potential of nerve since the U wave occurs coincident with the super-normal phase of ventricular excitability. (4, 129, 130, 132, 146)

Examination of the patterns produced by the electrical activity of the heart as recorded by the arrangements of electrodes employed in clinical practice may enable the interpreter to determine: 1) the cardiac mechanism (sinus rhythm, auricular flutter, etc.); 2) the presence of myocardial changes (as ischemia or death); 3) the presence of defects in the conduction of impulses in the heart; 4) the presence of abnormal electrolyte concentrations or the effects of such drugs as digitalis. (5) Most abnormal patterns are not characteristic of an etiologic type of cardiac disease but are only indicative of myocardial damage, expressed in disturbances in the order of depolarization and repolarization. Furthermore, most systemic diseases and many normal physiologic states are associated with unusual ECG patterns. (131) There have been many descriptions of the electrocardiographic changes in systemic disease (133, 134), but such claims have not always been supported by the experiences of others. (13)

ELECTROCARDIOGRAPHIC EVIDENCE OF MYOCARDIAL INFARCTION

The first electrocardiographic study of myocardial injury was made in 1909 (136) when it was found that the T wave is changed from positive to negative on injecting silver nitrate in the heart muscle. The following year it was observed (137) that the R-T segment becomes elevated after traumatization of the apical portion of a frog's heart. The next report on this important subject appeared in 1918 (138) when R-T segment changes occur on ligature of a coronary artery in dogs as well as in such cases in humans. (139, 140, 141) Other changes in infarction were described, as were attempts to correlate these changes with the location of the infarct. The importance of chest leads as well as limb leads for accurate diagnosis was emphasized (130) and studies showing the influence of factors other than infarction were published. (142, 143)

The pathologic changes brought about by infarction are discussed elsewhere in this paper. From the viewpoint of electrocardiographic interpretation, the structural changes resulting may roughly be divided into three zones: a central zone of dead heart muscle; a surrounding zone of partial destruction; and an outermost zone of ischemic but otherwise normal heart tissue. (3, 4, 96)

These zones, of course, are not clear cut but the division is a useful one in clinical electrocardiography. The alterations in electrocardiographic tracings resulting from infarctions can conveniently be considered as being due to the various influences of these zones.

Inasmuch as the innermost zone consists of dead tissue, the spread of normal depolarization is impeded or interrupted entirely depending on the size of the infarcted area. The deforming effect of the "dead zone" is thought by some investigators, notably Grant (3), to be limited to the first 0.04 second of the QRS complex; in fact in 90% of cases to be seen in exactly that time period, a great convenience to both pattern and vector readers.

The zone of injury surrounding the necrotic area is endowed with special electrical properties resulting from the electrophysiologic changes occurring in it and, since it is relatively electronegative compared to the surrounding normal heart tissue, produces a "current of injury" which may be detected even in diastole (transiently at the time of injury) when the heart is normally isopotential.

The ischemic area is mainly responsible for disturbances in the repolarization process (165) thus causing T wave changes that are observed in infarction.(3)

Such changes are not specific of myocardial infarction. They may occur in other conditions if inflammation, toxicity, trauma or other conditions producing "ischemia" are present. (144, 145) The T wave is also modified by the zone of injury; this deformity is not commonly of the same character as those caused by other pathologic states. (14)

The term "ischemia" is in many respects unfortunate, for it implies that the electrical changes are dependent on an actual diminution of myocardial blood supply. Such is not the case for there are numerous other noxious influences (some noted above) that can produce this electrocardiographic picture and yet that do not involve ischemia in the true sense of the word.(96)

The changes alluded to above are due to changes in the electrical properties of the injured tissues, consisting principally of: 1) a decrease in the degree of polarization of the cellular membrane in the affected zone; and 2) loss of the dielectric properties of the membrane. (96, 107)

When a cardiac muscle fiber is injured, its membrane is physiologically damaged, and the injured area becomes partially depolarized. (107) A continuum of change from normal to necrotic tissue can be demonstrated to exist. (146, 162) Between these two extremes there

are different degrees of polarization. The step-wise decrement of physiologic and electrical properties implies that there is a gradient of polarization rather than abrupt change. The changes in degree of polarization are variable but a correlation of electrical activity and histologic appearance of the involved myocardial tissue which is sufficiently accurate for present day clinical work can be made and has been noted above as the division of injured areas into three zones. (96)

Injured cellular membrane loses its dielectric properties, and charges which normally are separated by the membrane during electrical diastole now intermingle freely. The result is that a new, abnormal current (current of injury) flows between the injured and uninjured areas. This current flows during the entire cardiac cycle but for the sake of clarity it is helpful to discuss separately the electrical conditions that obtain during diastole and those that exist during systole.

The electrical diastolic period is that period of the cardiac cycle during which the tissues are at rest. During this time normal cells are polarized with a layer of positive charges on the outside of the cell and a layer of negative charges on the interior. With injury, the number of positive charges per unit of surface area is decreased. (96, 107) This area therefore becomes

relatively negative with reference to the intensely polarized surfaces of the uninjured portion of the heart. A difference in potential thus exists which is intensified by the effects of the loss of the dielectric properties of the injured cell membrane. Loss of the functional integrity of the cell membrane permits an unimpeded flow of ions and thus abolishes the normal dielectric characteristics. Although all normal myocardium contributes to this diastolic current of injury, the major source is that area contiguous to the injured portion. Diastolic current of injury is thus from the normal to the injured areas. The electrocardiographic effect of this current is discussed below.

The injury current during systole is of opposite polarity. The reasons advanced for this phenomenon are most likely that, as noted above, during excitation an actual reversal of polarization occurs with the result that a layer of negative charges comes to lie on the outside of the cell while a corresponding layer of positive charges is found on the inside of the cell. The voltage of the injured area after the activation wave (depolarization) has passed is thus strongly positive with respect to the external surfaces of the remaining normal tissue. (107)

An alternate explanation (148) holds that after muscle tissue has been injured, the waves in the tracing that follow activation do not exceed the pre-injury level of the isoelectric line. This explanation assumes that depolarization is not followed by a reversal in polarization and that all areas passed by the wave of excitation, injured and normal, have no potential, and therefore no current is generated. This concept explains the migration of the isoelectric (base) line as being due to neutralization of the diastolic current of injury by the activation wave.

Still other possibilities have been advanced (149) including a condition in which the injured area is not depolarized but which does not respond to the activation wave. Thus no diastolic current of injury is seen and a flow of current from the depolarized normal tissue to the polarized injured area is seen during electrical systole. A further basis is suggested as occurring in the situation of a partially depolarized injured area which does not respond to excitation and thus permits both diastolic and systolic injury currents to flow.

It is important to bear in mind that, unless records are obtained at the time of injury, the effects of the diastolic current of injury (manifested as a drop in the isoelectric line) are not detectable. (107) The

systolic effects remain and are useful in evaluation of infarctions.

Grant (3) divides the electrocardiographic abnormalities of acute myocardial infarction into four characteristic changes and states that all four may be present in a given case. Since he expresses these changes in terms of vectors and since the vector approach will be used to interpret the tracings in the cases cited in this paper, a brief comment on the vector method seems appropriate.

Any quantity of known magnitude and direction may be expressed as a vector whose symbol is a line whose length represents magnitude, whose spatial orientation indicates the direction of force and whose caret (arrowhead) indicates the sense of the force, in the case of electrical forces the location of electrical positivity. Since the electrical activity of the heart is associated with the movement of a fixed number of electrical charges (3, 96, 106, 107), the potentials generated by these processes can be measured and expressed as vector quantities. A correlation between electrical activity of the heart and the records obtained under standard circumstances becomes relatively simple.

Briefly, the electrocardiographic deflection in a given lead is a measurement (sufficiently exact for

clinical purposes) of the projection of the cardiac vector on the axis of that lead (hypothetical line joining the sites on the body surface where the electrodes for the lead in question are placed) at any instant in the cardiac cycle. Since the clinical electrocardiogram is a scalar delineation of electrical forces, measuring only magnitude (voltage) and sense (positivity or negativity relative to the orientation of the electrodes making up the leads), multiple leads comprising a coordinate axial system are necessary for expression of cardiac electrical activity as vector quantities. Comparison of the wave forms in two or more leads provides sufficient information to determine the direction of these electric forces. Although for strict accuracy all leads to be studied should be recorded simultaneously, the common method of serial transcription is adequate for clinical diagnosis.

The basic tenet of vectorcardiography is that all the electrocardiographic leads are derivatives of the spatial cardiac vector which is the vectorial notation of the equivalent heart dipole. (3) It is a manifest quantity and really a mathematical fiction because its true generator value cannot be determined directly at present although it can be estimated with the aid of a model of any given subject. (149, 150, 153) Furthermore,

the potential differences recorded at any electrode site from moment to moment are determined by the summation of all the electromotive forces generated by all parts of the heart from moment to moment, i.e. by the spatial vector. (151, 152) They are not essentially or chiefly reflections of local subjacent myocardial potentials (the proximity potentials of Wilson). (154, 155)

Since the heart which generates the electromotive forces lies in the body and sends its impulses through the surrounding conducting tissues (the volume conductor of Einthoven), the vector representing the forces at any given instant is oriented in three dimensional space. If one constructs a line connecting the ends of successive instantaneous vectors, the result is a loop which must be described in three planes. Although methods for directly recording this loop at present are not available (4), many devices for expressing this loop by indirect methods have been described. (156, 157, 158)

The heart is certainly not a real dipole (158) and investigation is now in progress to determine the electrical center of the heart (159, 179) and to develop special leads which will be relatively insensitive to the effects of motion of the dipole during the cardiac cycle. (158, 159, 160, 161) Also, the usual clinical records are obtained by serial recording of single leads

and the possibility of error due to changes in the myocardium during recording exists. (96)

The ECG as a diagnostic tool in study of infarction is limited almost entirely to infarction of ventricular tissue. In the atria it is possible that injury is more frequent than suspected but is obscured by the fact that the final atrial deflections are simultaneous with the initial ventricular deflection and the displacement of the P-R segments are usually not marked. (147, 162, 163)

It is convenient at this point to review the main anatomical features of the conduction system in the normal heart. It has been known for many years (96) that the stimulus which releases the necessary electromotive force for activation of the heart arises in the sinoauricular node (S-A node; node of Keith and Flack), then travels through the atria to reach the atrioventricular node (A-V node; node of Aschoff and Tawara), thence traverses the bundle of His with its right and left branches and ultimately reaches the ventricular muscle by way of the Parkinje system. (38)

Earlier in this paper a brief correlation between electrical events in the heart and the waves and segments of the scalar electrocardiogram was given. It remains only to state the commonly accepted normal values for

the duration, orientation and amplitude of the important waves and intervals.

The P wave (atrial excitation) normally has a duration of about 0.08 seconds and rarely is more than 2 mm. in amplitude on any of the limb leads. It is often biphasic in leads V_1 and V_2. Thus the first part of atrial activation produces forces which are slightly anteriorly directed while posteriorly directed forces dominate the remaining portion. (3)

The QRS interval (ventricular excitation) in the adult normally measures 0.08-0.09 seconds when measured at the longest complex in any limb lead. The direction of the mean QRS vector is determined by the ventricular mass and tends to point toward the center of mass of the ventricles. In normal adult subjects a vector pointing leftward, inferiorily and slightly posterior is seen. The direction of the mean QRS vector varies with the age of the patient, gradually swinging from a nearly horizontal rightward direction at birth through the slightly leftward and interior orientation of infancy to the leftward and interior (or vertical to slightly rightward) position of young adulthood. Beyond the late twenties, body build plays a more important role in determining the direction of the mean QRS vector. In tall lean persons it may be quite vertical; in obese, stocky subjects it

tends to be horizontal. In the normal patient of "average" body build this vector tends to swing leftward with advancing age because of the gradually developing left ventricular predominance, anatomically and physiologically, in the adult. (3) The amplitude of the tallest wave of the QRS complex should measure 6 mm. in at least one of the standard limb leads. The R wave usually measures between 5-15 mm. with the range of normal going to 28 mm. in the standard limb leads. The voltage is regarded as high if the highest QRS deflection exceeds 25 mm. in the bipolar limb leads, (I, II, III), 20 mm. in the augmented limb leads (aVR, aVL, aVF) or 50 mm in any of the conventional precordial leads. (4).

Normally the T vector (ventricular repolarization) varies less in direction in the frontal plane than does the mean QRS vector. Its migration with increasing age is less marked than that of QRS. In infancy it points leftward and markedly posterior, gradually shifting to a position more or less parallel with the frontal plane by about age thirty. Beyond this age it tends to be still more anteriorly directed. (3) Its duration is measured; the time for its inscription is included in the Q-T interval, which is measured in the lead where it is most clearly demarcated and, usually, in which it is longest. The Q-T interval (onset of QRS to end of T)

varies inversely with heart rate. The normal Q-T interval may be calculated from Bazett's formula: Q-T = K $\sqrt{R-R}$ in which K is a constant (0.37 for children and men and 0.40 for women) and R-R represents the interval between two R waves. The amplitude of T averages 2mm. in I, 3 mm. in II and 1 mm. in III; in precordial leads the waves usually range between 3 and 8 mm. (4)

The angle between the mean QRS and the mean T vectors (according to Grant (3)) is perhaps the most sensitive method so far devised for interpreting the T wave because it studies the forces generated during repolarization in terms of depolarizing forces and expresses this relationship in a quantitative form. In the normal subject the angle between the mean spatial QRS vector and the mean spatial T vector is quite narrow, not often exceeding 45° in the frontal plane or 60° in the antero-posterior plane.

The P-R interval (onset of P to onset of QRS) represents conduction time in S-A node, atria, A-V node and sufficient ventricular conduction system to excite a measurable ventricular excitation. (3) It generally has a duration of 0.12-0.20 seconds in the adult whose heart rate ranges between 60 and 80/minute. With more rapid rates (100-120/minute) 0.18-0.19 seconds is the normal upper limit. (4) This interval tends to increase

from the 0.10-0.12 second value of childhood to adult levels in a manner similar to that described for the waves noted above.

The four abnormalities found in infarction, according to Grant (3), are: 1) an alteration in direction of the instantaneous vector of the first part of the QRS interval; 2) a change in direction of the mean T vector; 3) the presence of an S-T vector; and 4) an abnormal direction of the terminal vector of the QRS interval. The reasons for these changes are discussed below.

Alteration in direction of the first portion of the QRS complex is usually expressed as the direction of the mean vector for the first 0.04 seconds of the QRS interval. (3) This change results from the loss of vector contributions from the subendocardial layers at the site of infarction since this area is electrically inert. (164) As a consequence of this "dead zone effect", the initial 0.04 seconds vector tends to point away from the infarcted area. Since in the great majority of cases of myocardial infarction the infarct involves primarily the left ventricle, any initial 0.04 second vector which points away from this region should arouse suspicion that an infarct is present in this area. (3) The presence of left bundle branch block obscures the first 0.04 vector and complicates the vector approach to infarction.

Pattern methods (165, 166) have been suggested in this instance. An illustration of this problem is included in the cases to be discussed.

There is no evidence that the particular electrical location of an infarct necessarily coincides with its anatomic location. Three reasons are offered as to why this is so.

1. The electrical and morphological effects of infarction are different manifestations of this process and may depend upon different biochemical or physical aspects of the infarcted membrane. (80, 167)

2. Many patients with this disease prove at autopsy to have had multiple infarctions. (166, 168, 169) Since the electrical abnormality results from the effects of all infarcts wherever they lie, the initial 0.04 second vector may be of no value and may even point away from an entirely uninvolved region of the heart. (3)

3. The characteristics of the initial 0.04 second vector prior to infarction may influence considerably the amount of deformity following infarction. (3) A subject whose pre-infarction initial 0.04 second vector was vertical would exhibit a different alteration in this vector than would a subject whose pre-infarction initial 0.04 second vector was horizontal.

This criterion is seldom sufficient to establish the diagnosis of infarction and, in borderline cases especially, additional clues, clinical or laboratory, must be present for accurate evaluation of the patient.

The change in direction of the mean T vector is due to so-called electrical ischemia in the tissues surrounding the infarct. (3) The relative electronegativity in the ischemic area produces a mean T vector which points away from the injured area. Thus the initial 0.04 second QRS vector and the mean T vector tend to have the same direction in each lead in infarction.

The current of injury (discussed above) produces an S-T vector which points toward the site of infarction and thus tends to be opposite in direction to the 0.04 second QRS vector and the mean T vector in cases of infarction. Paradoxic motion of the infarcted ventricle and aneurysm formation have been suggested as possible causes of persistance of the S-T vector for more than six months following infarction. (4, 90) Since the infarcted area is by this time entirely converted into dense fibrous tissue, it is unlikely that remaining S-T charges are due to the so-called current of injury. (3)

Peri-infarction block has been suggested to be due to a delay in the wave of depolarization the area overlying a subendocardial infarct. (170, 171)

Because the infarcted area cannot conduct the impulse of depolarization, the stimulus must spread around the injured area to reach the overlying relatively normal epicardial tissue. This delay in conduction is seen in the acute stage of infarction (3), but more commonly occurs hours to days afterward. Peri-infarction block is thought to account for the changes in the terminal 0.04 second QRS vector in the cases with little or no prolongation of the QRS interval. In peri-infarction block the vector (terminal 0.04 second QRS) tends to point toward the site of the infarct since the tissue surrounding this area is the last to be depolarized in such cases. The transitory character of this phenomenon may be due to the inability of the few muscle cells capable of depolarization to contribute sufficiently to the total electrical field of the myocardium. (170)

Although in most cases of acute infarction all four vector abnormalities may be demonstrated (3), cases in which severe or even fatal infarction have occurred with no electrocardiographic abnormalities whatever are reported. (9, 125)

A hyperacute stage has been described as occurring during the first few hours following myocardial infarction in man. (3) This is rarely seen in clinical practice because it is so short lived and is usually replaced by the

more familiar changes described above before electrocardiographic studies can be obtained. The hyperacute stage is characterized by increased magnitude of the S-T and T vectors, which are parallel and pointing toward the site of the infarct. Rarely this may persist for two to three weeks before the T vector rotates to the position found more commonly. The occasional delay in T wave rotation makes the suggestion that hyperacute changes are due to local release of potassium ion highly unlikely.

A rather general approximation of the age of an infarct may be obtained by recalling that the S-T vector is present only in the acute stage, subsiding within a few weeks. The mean T vector gradually rotates in a period of months following the acute stage, finally reaching either a "normal" position or that orientation conventionally ascribed to left ventricular ischemia. The initial 0.04 second QRS vector less frequently returns to a "normal" position although this may also occur as months pass following infarction. Sometimes a suspicion of infarction may arise when the later vectors in the 0.04 initial vector return to normal so the Q waves (so dear to pattern readers) become shorter, or, less often, when the first QRS vectors return to normal, producing a tiny R deflection prior to the Q suggestive of infarction.

The terminal 0.04 second vector least frequently returns to a normal direction. (3) Thus in cases of old infarctions, the only electrocardiographic abnormality may be a QRS deformity: the initial 0.04 second vector, the terminal 0.04 second vector or both. (172)

The electrocardiograms used as illustrative material in this presentation will be interpreted by the methods advocated by Grant. (3) Cardiac vectors are obtained with sufficient accuracy for clinical use by this or other methods using scalar records only. (173) Electrocardiographic diagnosis using the pattern approach (174, 175, 176) will not be attempted as it is felt that this method is considerably more empiric. Identification of S-T and T vectors by comparison with the level of the preceding and following P waves will be practiced in interpreting the tracings to be discussed. This method is suggested as being more accurate than the usual comparison of S-T and T with the level of origin of the QRS complex. (177)

The spatial vectocardiographic approach using a Cathode Ray Oscillograph and a high speed camera is still relatively new and will not soon replace the conventional scalar records. (152, 178, 179, 180, 181, 182) The bulkiness of the equipment necessary for such recording and the expense associated with its use together with the

present limited number of studies using the method (relatively crude diagnostic criteria) operate to prevent its early clinical use. Small, relatively inexpensive models have been developed (157), but have not found widespread acceptance. It is chiefly useful at present in recognizing the residual effects of myocardial infarction when more subtle (0.01 to 0.02 second) degrees of deformity of QRS complexes may be determined than possible with the conventional methods of recording. (181) It is of little value, comparatively speaking, in diagnosis of arrhythmias. The vector concept is well established in electrocardiographic theory and combinations of conventional scalar leads are commonly used to derive the spatial orientation of various portions of the vector loop of myocardial excitation and repolarization.

Electrocardiography in the infant and child will not be discussed in this paper. Infarction of the myocardium in this age group is sufficiently rare (19)to justify this exclusion. The principal value of the electrocardiogram in the pediatric patient lies in the aid in recognition of congenital abnormalities which it provides. (70)

Illustrative Cases

The cases presented are taken from the records of Bishop Clarkson Memorial Hospital, Omaha. In each instance a brief clinical history, electrocardiographic studies and post mortem examination findings will be noted. No attempt to convey relative magnitudes of vectors will be made. It is not the purpose of this sample to serve as a subject of statistical analysis. The cases merely illustrate certain of the problems encountered in clinical electrocardiography. The ensuing discussion will be based upon the texts of Grant (3), Friedberg (4) and Sodi-Pallares. (19)

Case 1 is an example of the change which infarction produced in a subject for whom a previous "normal" record was available. Figure 1 is a record obtained when the patient was 61, three years prior to his death. It was interpreted as being within normal limits. Figure 1a is the vector representation of this tracing. Ten months prior to death, tracings (Figures 2 and 2-a) showed an apparently recent infero-anteroseptal infarction. Figures 3 and 3-a show the final record obtained, four days before death. This record shows both old and recent inferoseptal myocardial infarction.

At the terminal illness the patient was 64 years old. He was admitted to the hospital with a history of hematemesis, melena and syncope. He was apprehensive but apparently in no distress at time of admission. BP 120/52; Pulse 72, reg; lungs clear to auscultation and percussion. The apical rhythm was regular and no murmurs were heard. The liver was 4 fingerbreadths below the right costal margin. Admission lab. studies: Hb 10.9; RBC 3.9 million; WBC 13,100 with normal differential. Admission transaminase (SGO-T) was 15 units, rising to 90 units two days later. Admission diagnosis was bleeding duodenal ulcer. He complained of intermittent chest pain but had no dyspnea. He developed a sinus tachycardia two days after admission. On the day before death he lost the use of his right arm and hand and drooled from the right corner of the mouth. He died on the sixth hospital day.

Autopsy examination of the heart revealed a moderately dilated, 590-gram heart with a yellowish-brown discoloration of the myocardium beneath the endocardium together with thinning and out-pouching of the apical portion of the left ventricular wall and lower interventricular septum. Patchy calcification of the left and right coronary arteries together with several areas of old and recent thrombus of the right coronary artery

2.5 cm. distal to its origin was noted. Histologic studies demonstrated both old and recent infarction in the interventricular septum and marked atheromatous thickening of the wall of the left coronary artery with stenosis of its lumen. The right coronary artery contained an occlusion 2.5 cm. distal to its origin by recent thrombotic material together with hemorrhage into an atheromatous plaque. Adjacent segments showed old, recanalized thrombus.

In this case the electrocardiograph was able to record changes diagnostic of the conditions later found at autopsy.

Case 2 illustrates peri-infarction block and complete A-V block. Figures 4 and 4-a are taken from a record obtained 6 months before death. Figures 5 and 5-a were obtained from a tracing taken 5 days before death.

The patient at the time of his terminal illness was 65 years old. He complained of pain in the epigastric region (treated for duodenal ulcer 6 months previously) and stated that his blood pressure had been high for several months. Physical examination revealed the lungs to be clear to percussion and auscultation. The heart rhythm was irregular at 60/min. Generalized

tenderness of the upper abdomen was present and the liver edge was felt 4 cm. below the right costal margin. Admission BP: 250/98; WBC: 12,800 with normal differential; Sed. Rate 38 mm/hr. Serum transaminase (SGO-T) rose from 30 to 130 units during hospital course. He died on the eighth hospital day following a gradual downhill course.

Gross examination of the heart at autopsy showed a weight of 460 grams. A patchy, fibrinous exudate covered the epicardium and pericardial sac. An irregular area of hemorrhage measuring 4 cm. at its greatest extent was seen on the posterior epicardial surface. This area was markedly soft to palpation. A recent infarction including a 2 cm. rupture in its mid-portion was found in the posterior portion of the interventricular septum. The remaining myocardium was thickened and contained multiple small foci of grayish-white tissue averaging 1 mm. in diameter. A recent occlusion of the right descending coronary artery about 3.5 cm. from its origin. The remaining coronary vessels were only slightly thickened and sclerotic.

Microscopic sections of the infarcted area confirmed its recent origin. An area of hemorrhage into the atheroma with rupture into the lumen together with marked thickening of the wall and stenosis of the lumen

of the right coronary artery was noted.

This case again shows the rather close correlation sometimes obtainable with clinical and pathologic studies of infarction.

Case 3 is that of a 71-year-old lady who entered the hospital with a history of longstanding hypertension together with dyspnea and wheezing and chest pains for about one month before admission. Physical examination revealed moist inspiratory rales in both lung bases; and an apical rate of 100/min. with frequent extra systoles; a grade I^{I} systolic apical murmur; BP 160/80; liver edge one finger breadth below the right costal margin and slight pitting edema of both ankles. A chest film at time of admission revealed left ventricular enlargement and bilateral pulmonary vascular congestion. Hb. 13.7; RBC 6 million; WBC 9,100 with normal differential count. She was treated for congestive heart failure but expired on the second hospital day. A single ECG was obtained. (See Figures 6 and 6-a.)

Autopsy findings include a heart weight of 360 grams and marked left ventricular preponderance. The coronary arteries are thickened and stenosed by calcified atheromatous plaques. The circumflex branch of the left coronary artery is occluded ½ cm. distal to its

origin by hemorrhage beneath an atheromatous plaque. No other occlusions were noted and it was observed that the circumflex artery contained blood distal to the point of occlusion. An area of infarction with yellow-gray fibrosis and numerous petecheal hemorrhages was seen in the interventricular septum and similar changes were seen on the lateral and anterior surfaces of the left ventricle. No fresh hemorrhagic necrosis was seen. Figure 7 is a gross view of the heart as sectioned for this study and illustrates the method of gross exam employed.

Histologically the normal architecture of the heart is distorted by broad bands of hyalinized, fibrous connective tissue in which there is marked edema. The pattern was thought to be consistent with a myocardial infarction of several weeks duration.

In this case the infarction was not diagnosed on the original reading of the cardiogram. Through the retrospectoscope one can perhaps find sufficient evidence for this diagnosis on careful examination of the tracing.

Case 4 demonstrates the problem of diagnosing infarctions in the presence of bundle branch block. The patient was admitted with complaints characteristic of myocardial infarction and the tracing shown in Figures 8 and 8-a was obtained. The patient is a 53-year-old man who stated that he had a scarred heart valve and who

was found to have dyspnea, chest pain, moist basilar rales and a grade II apical systolic murmur. Moderate pitting edema was noted in both ankles. Hb 12.5 gram; RBC 4.4 million; WBC 16,750; 1± albuminuria, trace of glycosuria, 10-20 RBC, pus cells and granular casts in the urine sediment. His hospital course was progressively downhill. Bloody sputum noted on day following admission. Several days of apparent improvement followed but he became cyanotic and displayed irregular pulse and breathing 8 days before death. The second record (Fig. 9) was obtained 3 days before death. He died on the 32nd hospital day.

At autopsy the heart weighed 650 grams. The pericardial surface was smooth and glistening. An area of softening 2 cm. in diameter was felt at the apex. A second area of softening was found to lie posteriorily at the junction of the left ventricular wall and the septum. This measured 6 cm. by 2 cm. and appeared to be an area of old infarction. An area of almost complete occlusion was demonstrated in the anterior descending branch of the left coronary artery 2 cm. below the bifurcation. This was thought to be due to atheromatous deposits noted in the remaining vasculature.

Microscopic exam shows only evidence of old infarction. No recent infarcts were found. The coronary

arteries were described as moderately sclerosed.

Case 5 illustrates the problem of determining the presence of the Wolff-Parkinson-White syndrome and the difficulty in identifying infarction in this conduction pattern. The patient is a 75-year-old male who had been hospitalized on numerous occasions over the year prior to demise because of dyspnea and cardiac decompensation and who gives a history of previous infarction. Three or four days before the final admission he had progressive dyspnea and marked orthopnea. Physical examination revealed a chronically ill, alert patient with marked respiratory difficulty. The cervical veins were markedly distended. The heart rate was rapid (150/min.) and regular. A grade III soft, blowing, apical, systolic murmur and marked cardiac enlargement to percussion were found. The lungs showed expiratory wheezes and dullness in the left base. A smooth, slightly tender liver edge was felt 5-6 cm. below the right costal margin, 1+ pitting edema of both ankles. Figure 10 is the ECG obtained at the last admission. Figure 11 was recorded on the day before death, which occurred on the fifth hospital day. Earlier records (from up to 12 years before death) show left ventricular hypertrophy and incomplete right bundle branch block, then inferoseptal infarct, then incomplete right bundle branch block disap-

pears, then anteroseptal and anterior infarcts.

Gross examinations of the heart showed a weight of 560 grams. There was marked distention of both ventricles and atria. The coronary arteries were markedly narrowed by atheromatous plaques which in many areas were calcified. The anterior descending branch of the left coronary artery was completely occluded by organized thrombosis which was partially recanalized. No other occlusions were demonstrated. A marked increase in vascularity of the heart with numerous small ramifications of coronary vessels was noted. The wall of the left ventricle averages 8 mm. in thickness but in some areas is thinned to 2-3 mm. The posterior surface contains numerous small, irregular plaques of fibrous tissue averaging 4-5 mm. in diameter. Sections of the muscle revealed a large amount of blood exuding from the myocardium itself.

Microscopic examination shows distortion of the myocardium by irregular broad bands of fibrous connective tissue in which are interspersed isolated myocardial muscle fibers, many of them extremely large. Other areas show loss of nuclei and granular cytoplasm. Foci of necrosis with perivascular neutrophilic infiltrates are also reported. The old and recent infarcts involve chiefly the anterior wall of the left ventricle and the

anterior portion of the interoventricular septum.

This case illustrates the value of pre-infarction electrocardiograms, the use of which would have simplified interpretation of the tracing which was available. This case may properly be considered as being of the electrocardiographically "silent" type although perhaps in retrospect one can identify sufficient evidence for infarction in the available records.

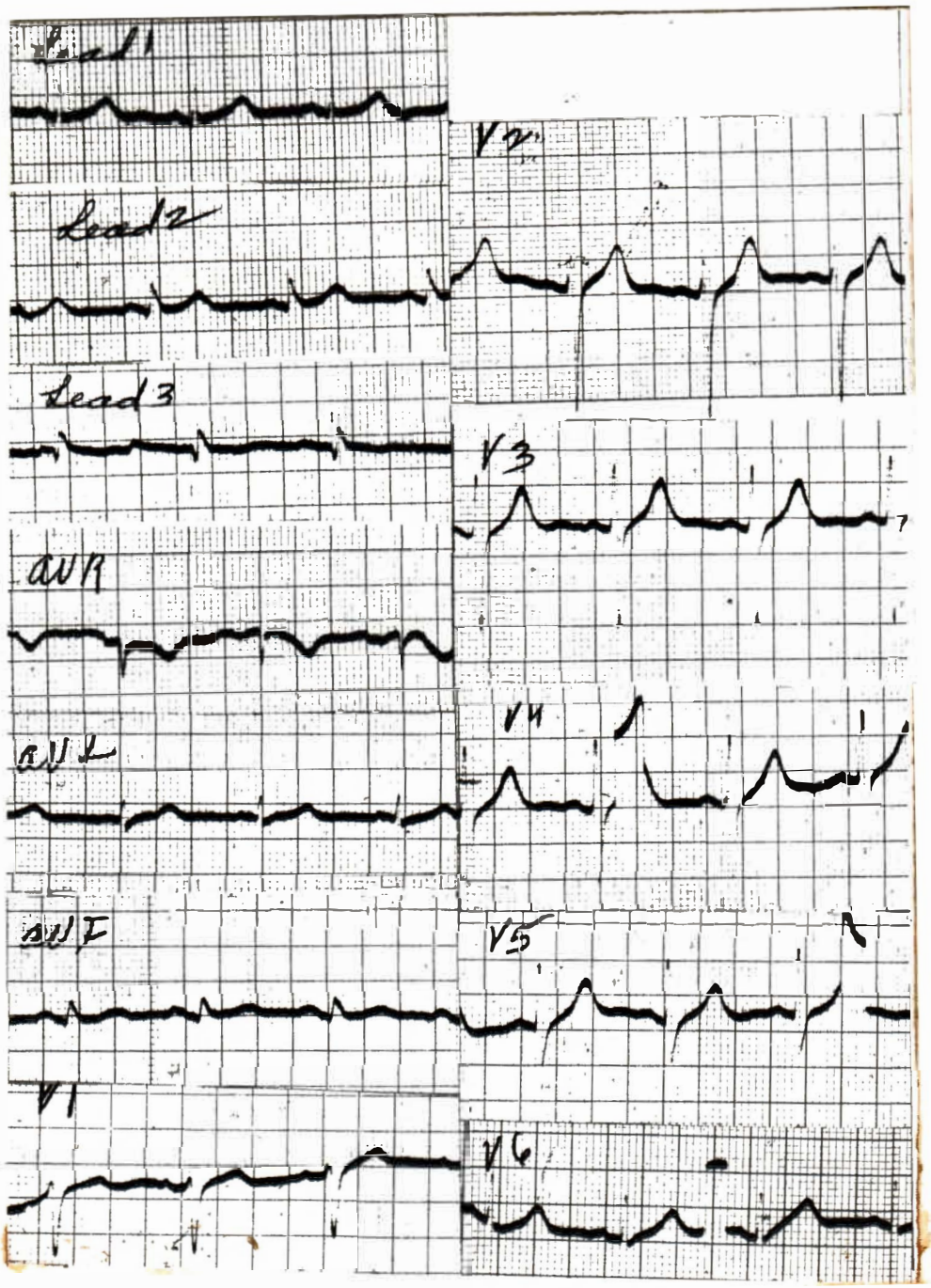

Figure 1. (self size)

Rhythm: Sinus

Rate: 79/min.

P-R: 0.16 sec.

QRS: 0.09 sec.

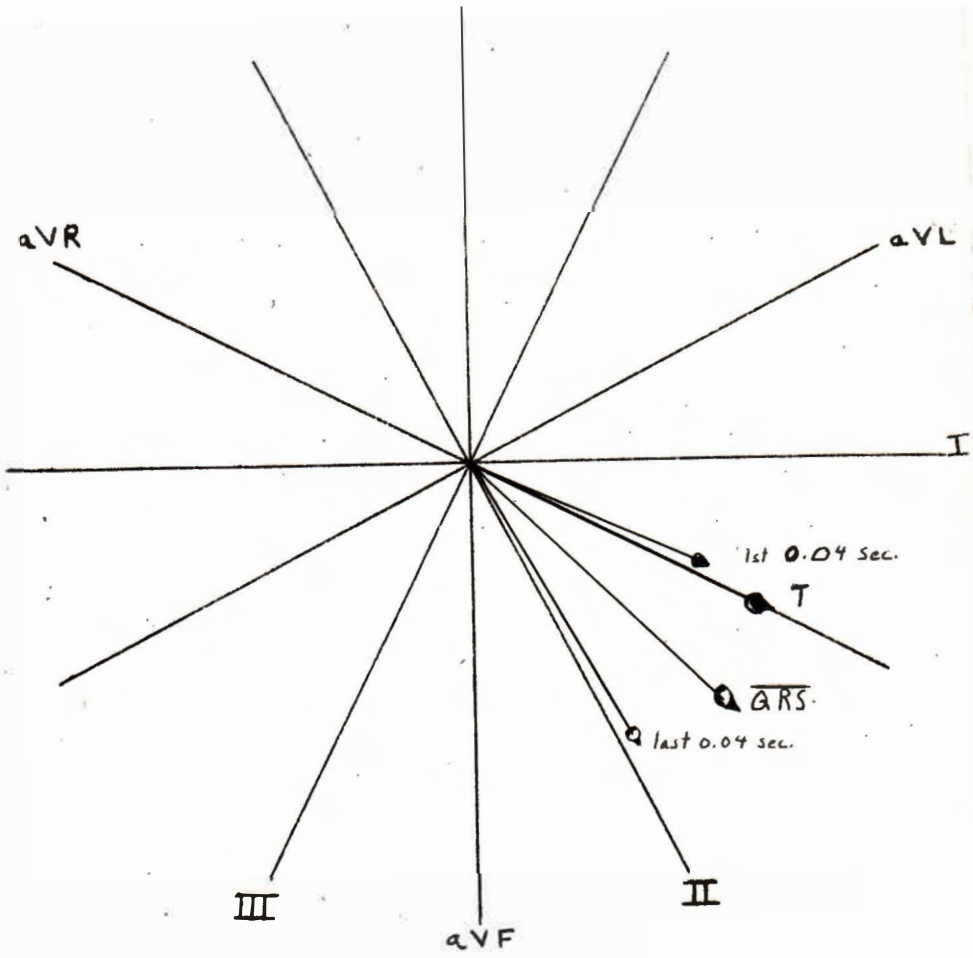

Figure 1-a.

Within normal limits.

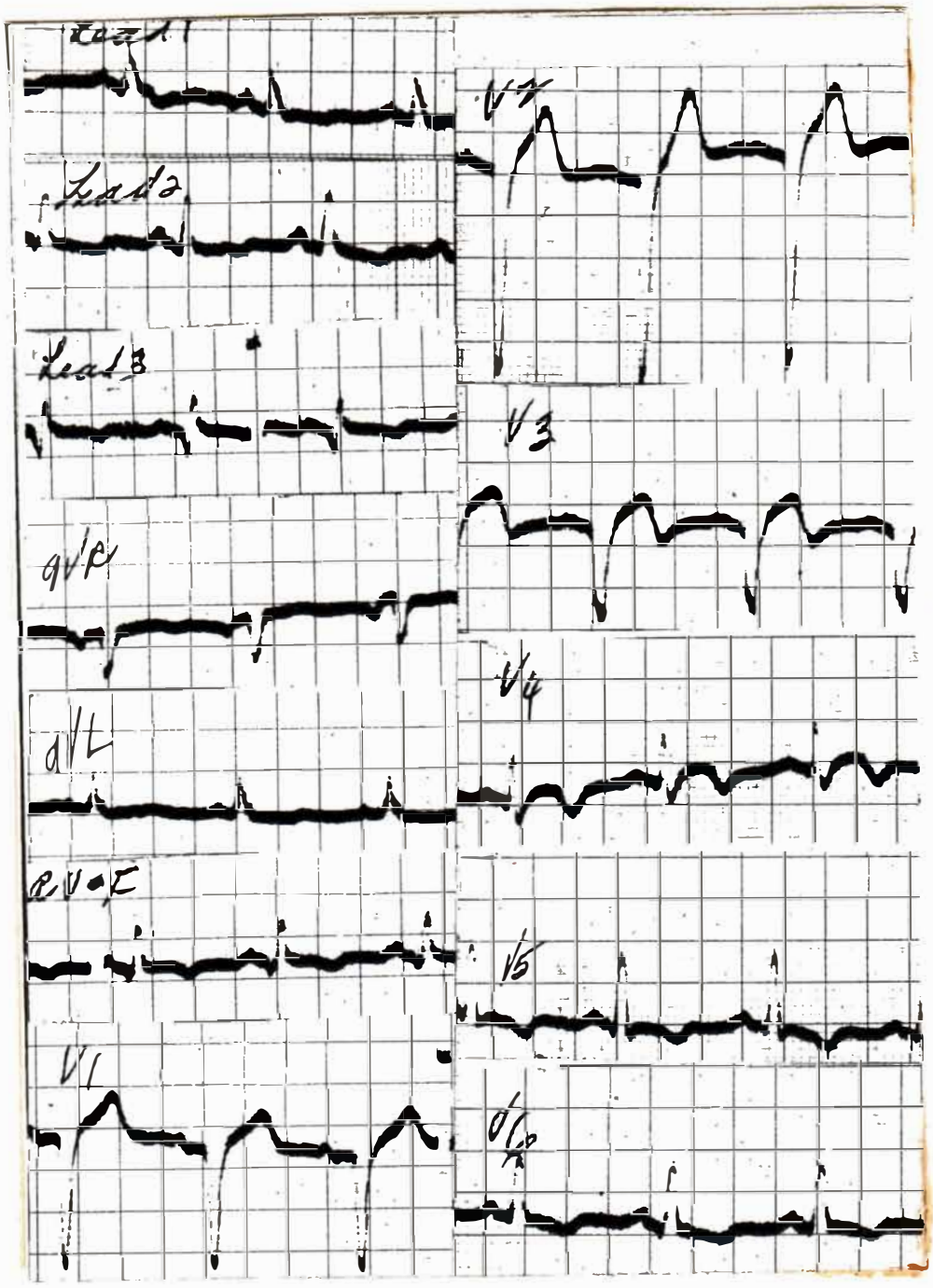

Figure 2. (enlarged 19%)

Rhythm: Sinus

Rate: 88/min.

P-R: 0.14 sec.

QRS: 0.10 sec.

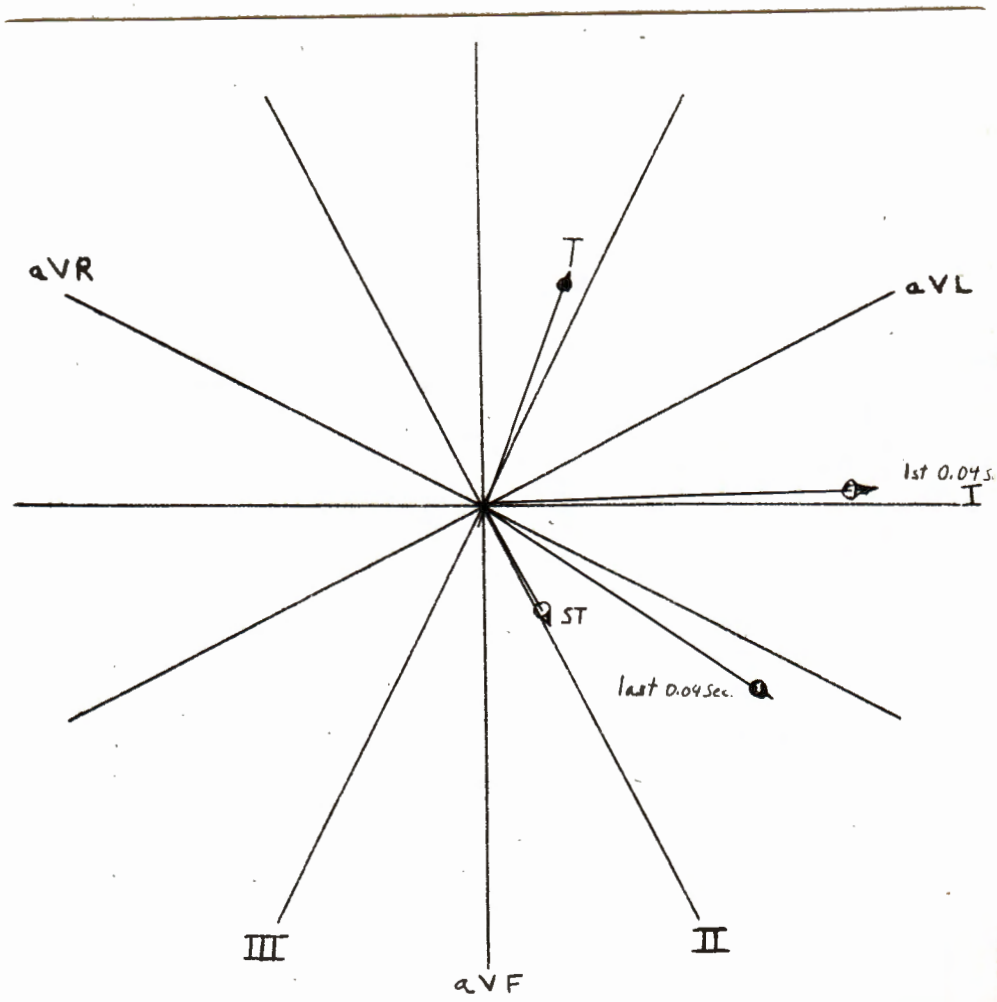

Figure 2-a.

Apparently recent infarction(s).

Anteroinferoseptal in location, possibly transmural since 1st 0.04 and last 0.04 sec. vectors are somewhat parallel.

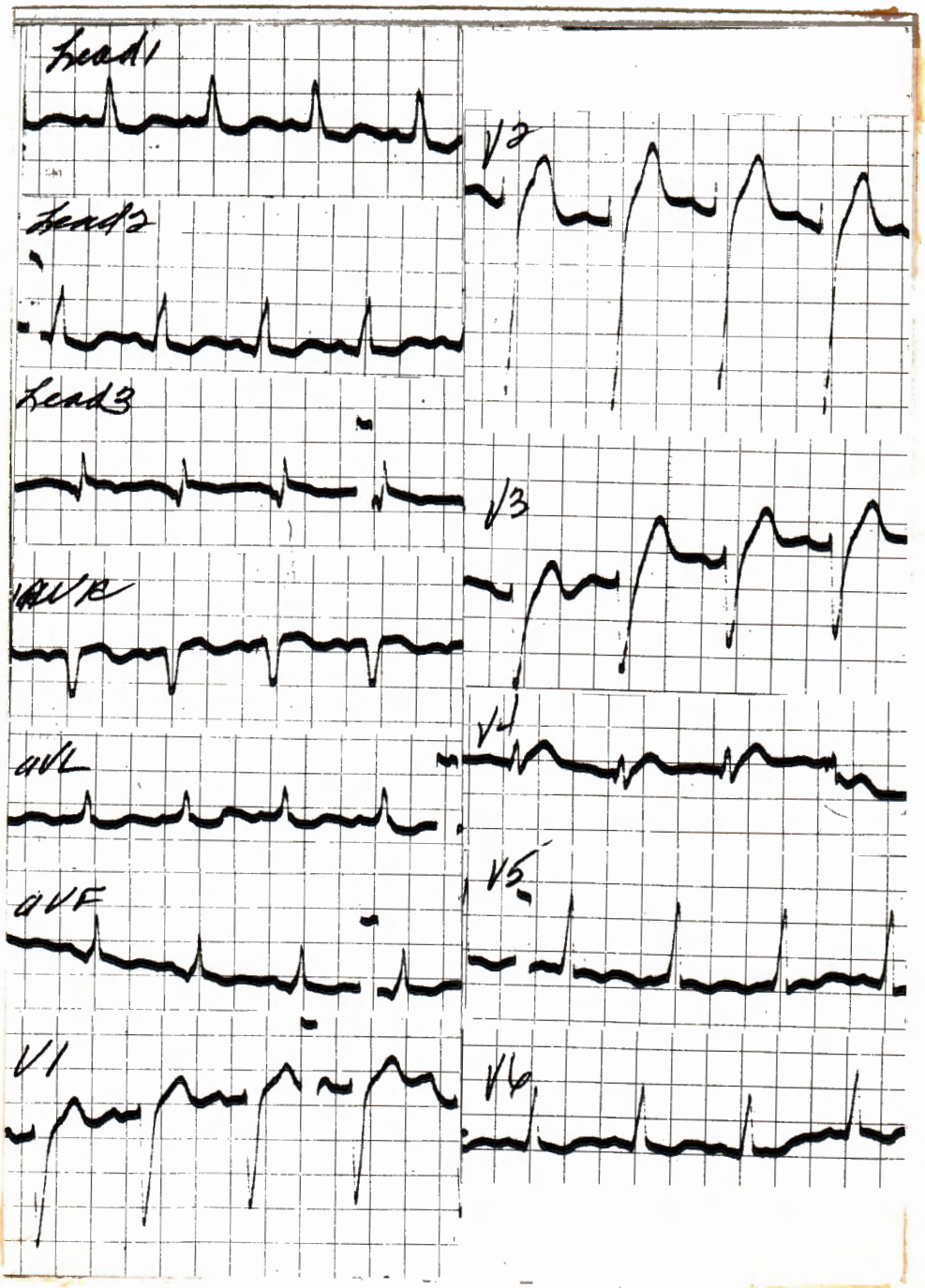

Figure 3. (2% reduction)

Rhythm: Sinus tachycardia

Rate: 103/min.

P-R: 0.15 sec.

QRS: 0.10 sec.

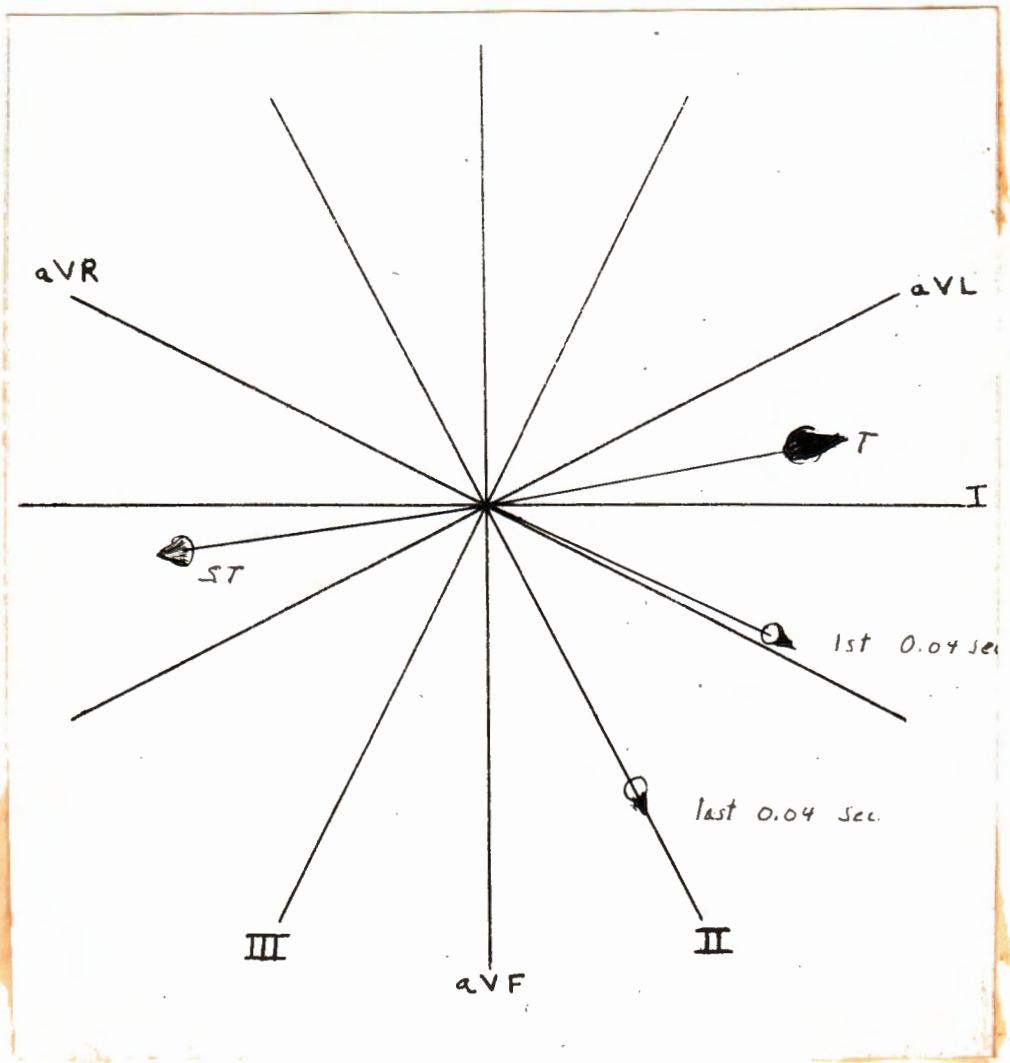

Figure 3-a.

1. Myocardial ischemia
2. Old anteroinferoseptal infarction
3. Possible acute inferoseptal infarction

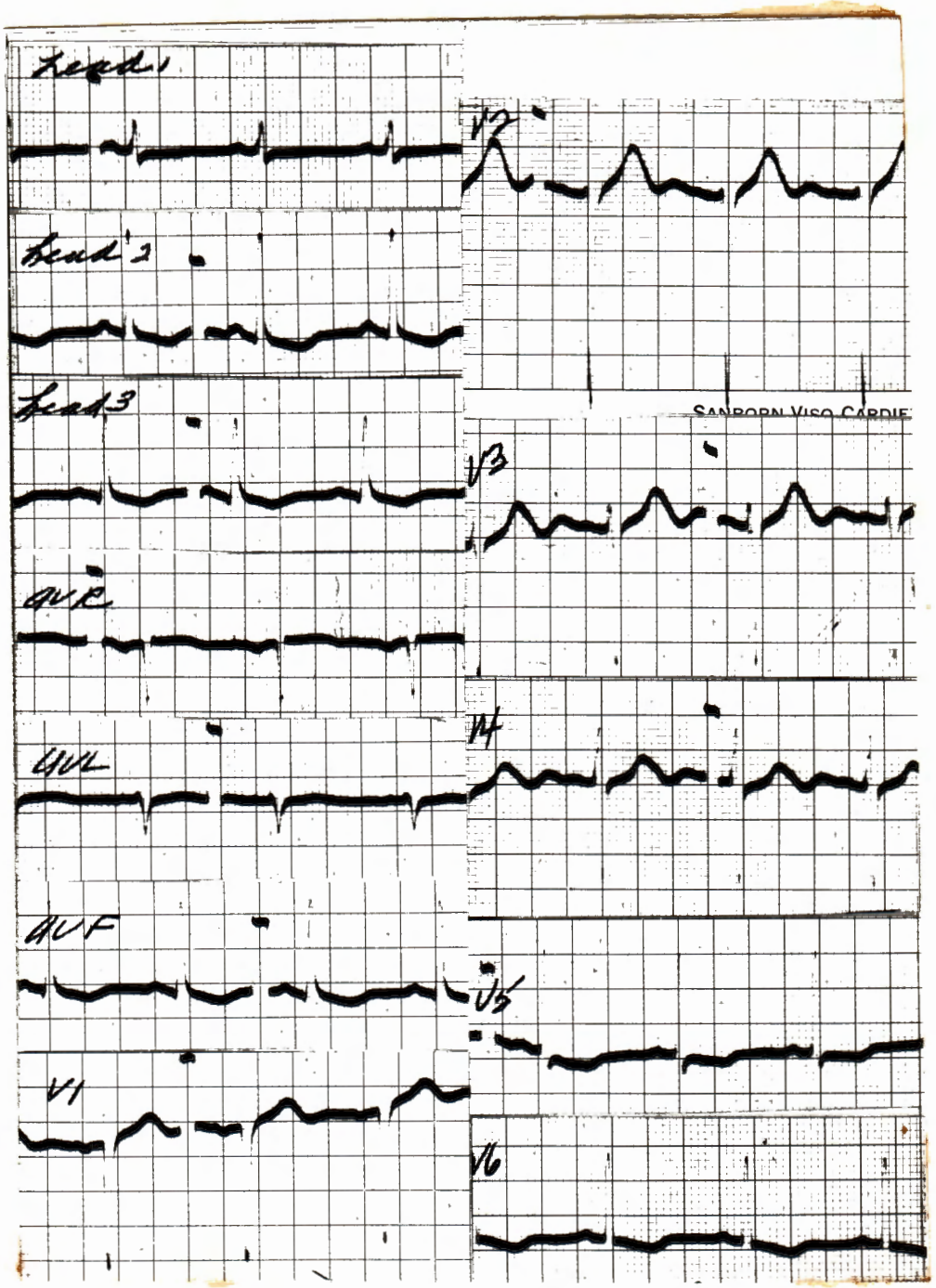

Figure 4. (self size)

Rhythm: Sinus

Rate: 80/min.

P-R: 0.14 sec.

QRS: 0.09 sec.

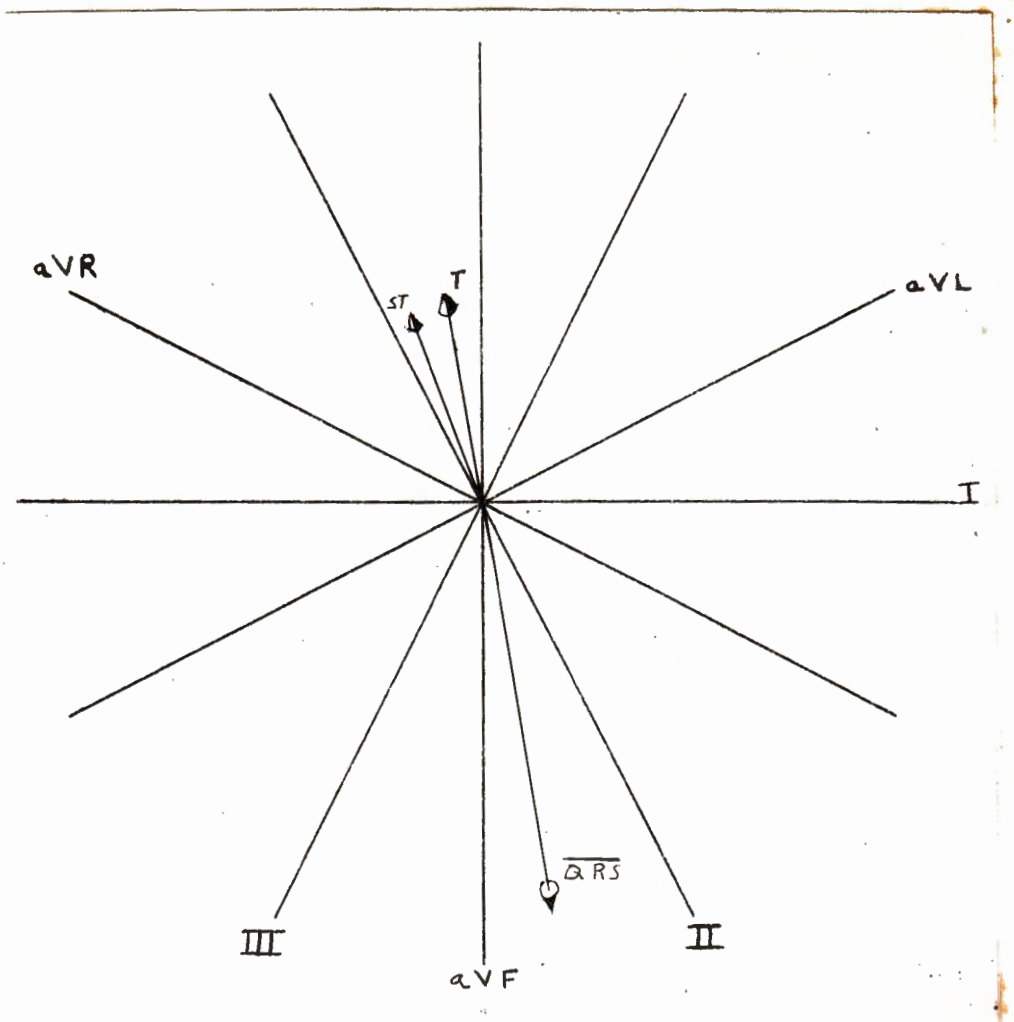

Figure 4-a.

Left ventricular hypertrophy.

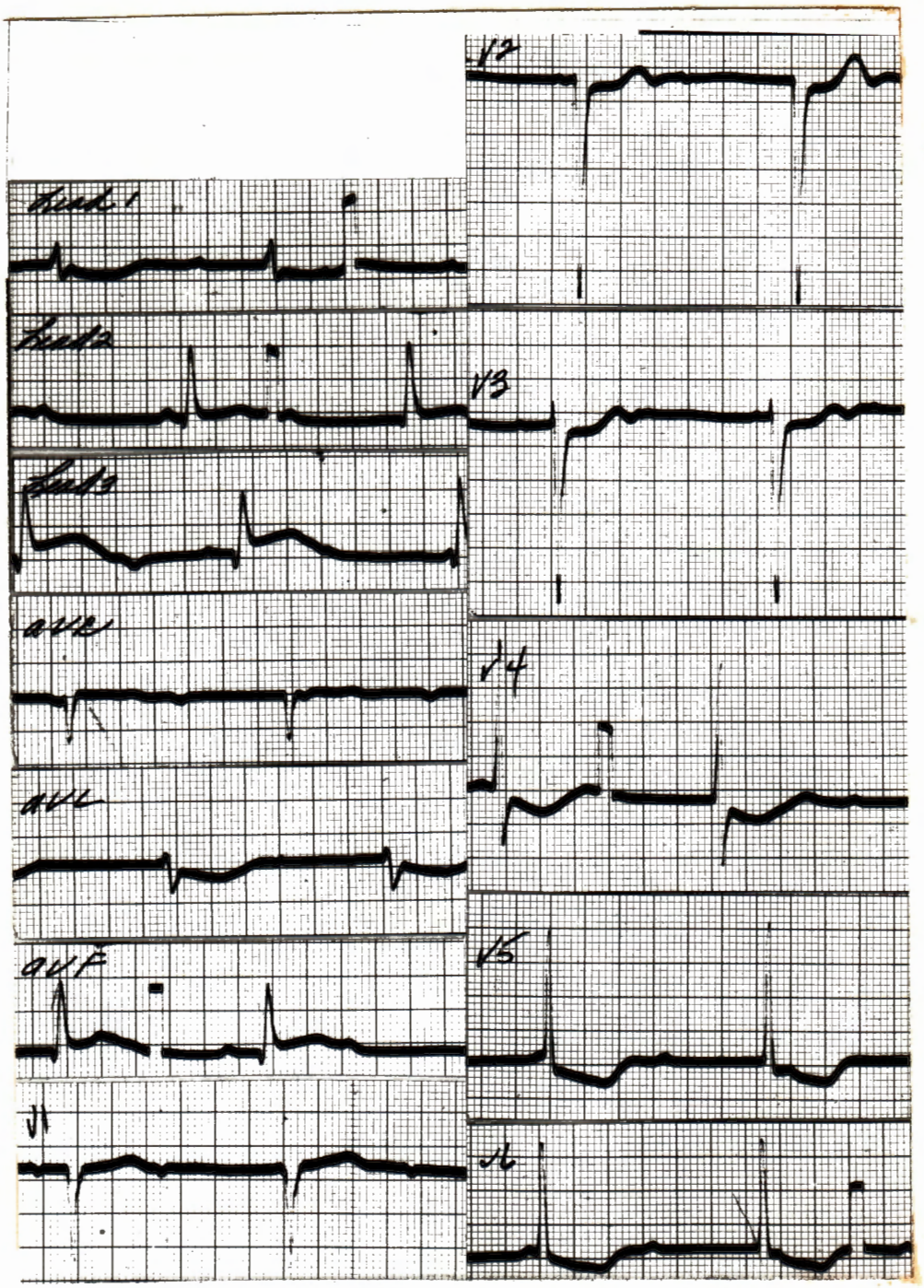

Figure 5. (reduced 3%)

Rhythm: Complete A-V block

Rate: Atrial 84/min.; ventricular 48/min.

P-R: Not applicable

QRS: 0.10 sec.

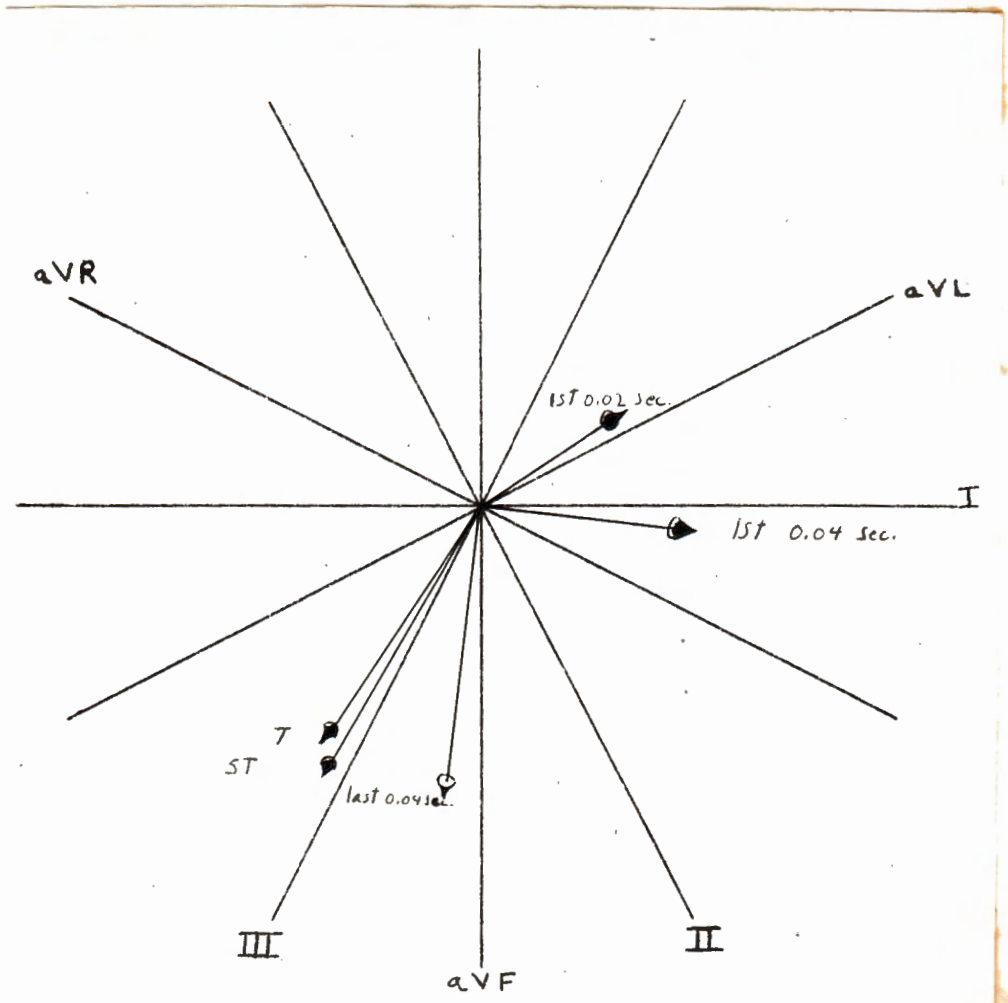

Figure 5-a.

1. Mild left ventricular hypertrophy
2. Acute inferoseptal infarction with peri-infarction block.

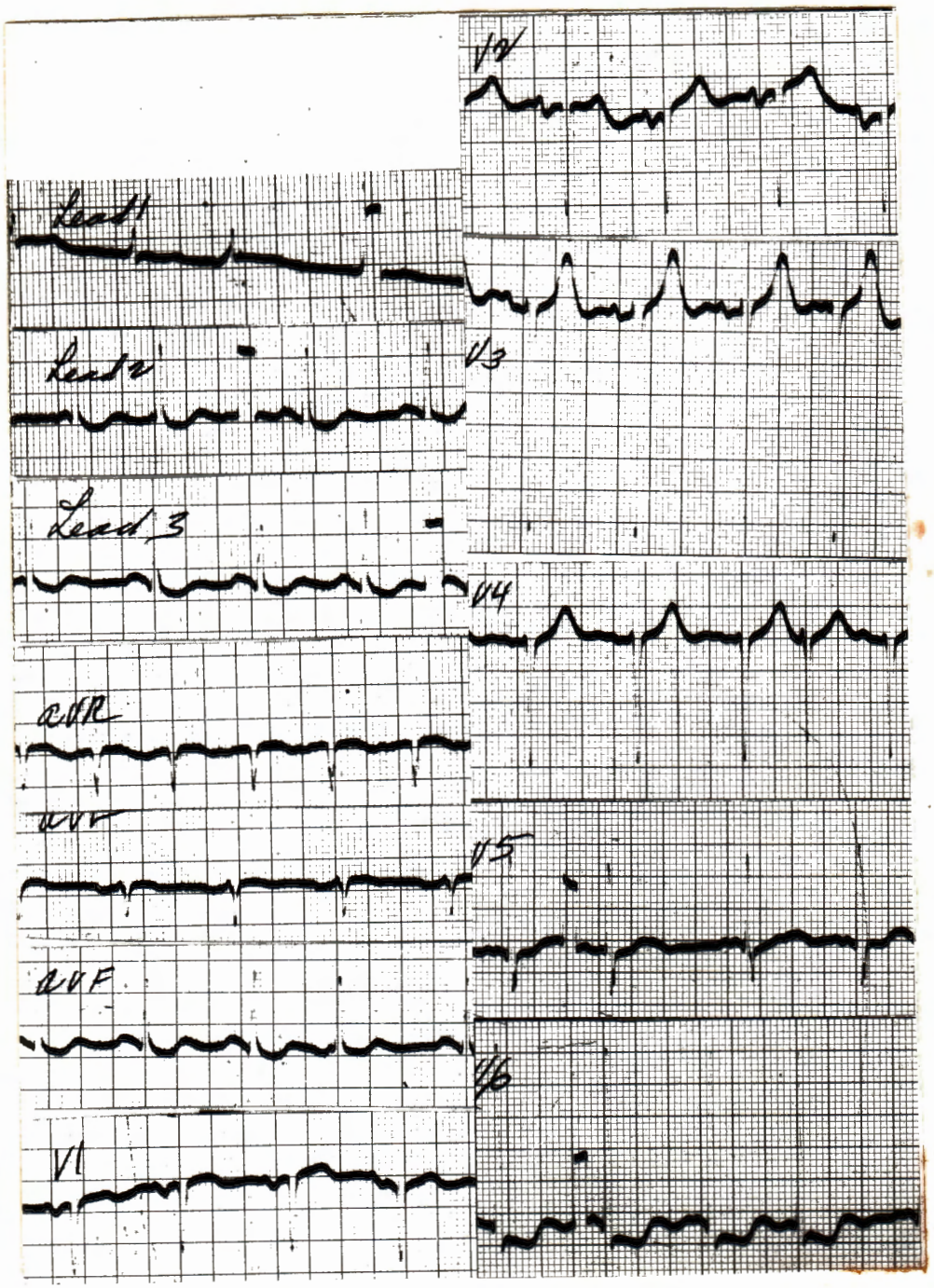

Figure 6. (reduced 9%)

Rhythm: Wandering Pacemaker with frequent atrial nodal and ventricular premature beats.

Rate: 100/min.

P-R: 0.14 sec.

QRS: 0.08 sec.

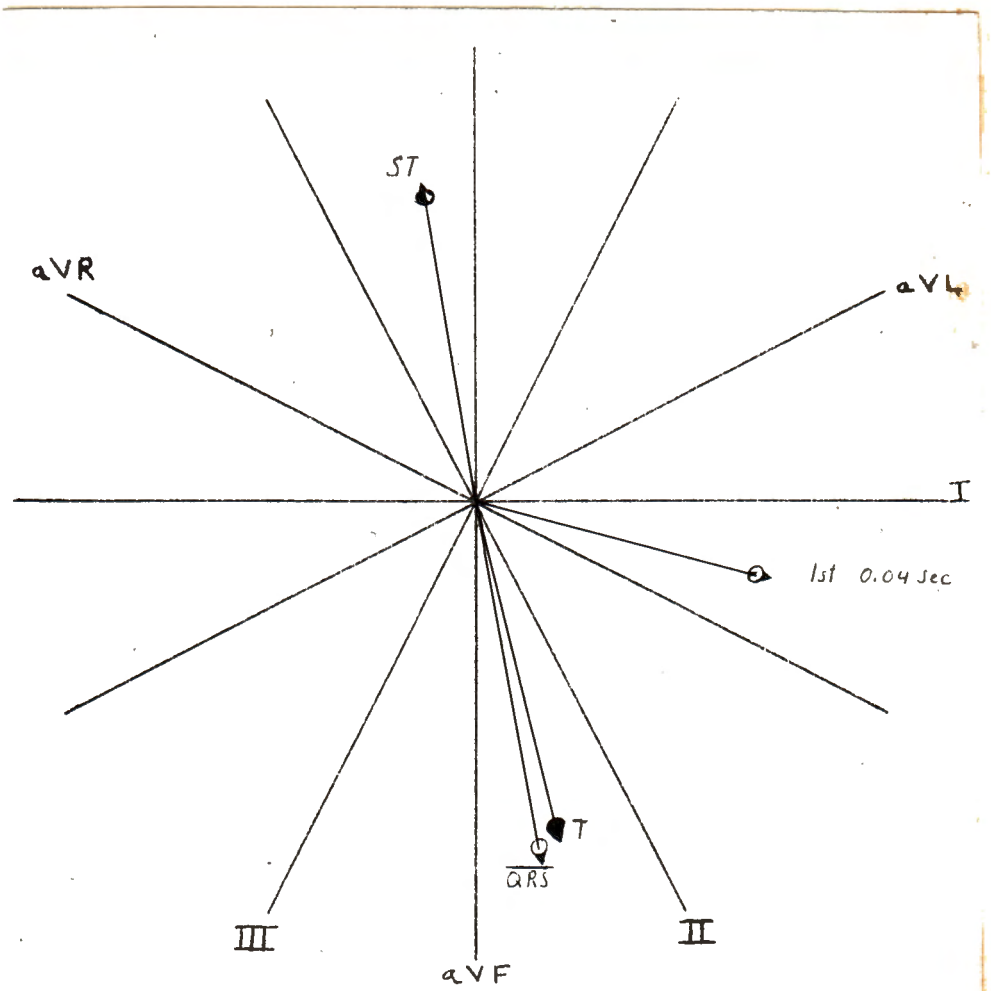

Figure 6-a.

1. Left ventricular hypertrophy
2. Left atrial hypertrophy
3. Digitalis effect
4. Possible myocardial ischemia

Figure 7. (rule is graduated at centimeter intervals)

Heart of Case 3 sectioned transversely to long axis showing pale areas of old infarction due to replacement of functioning myocardium by fibrous bands.

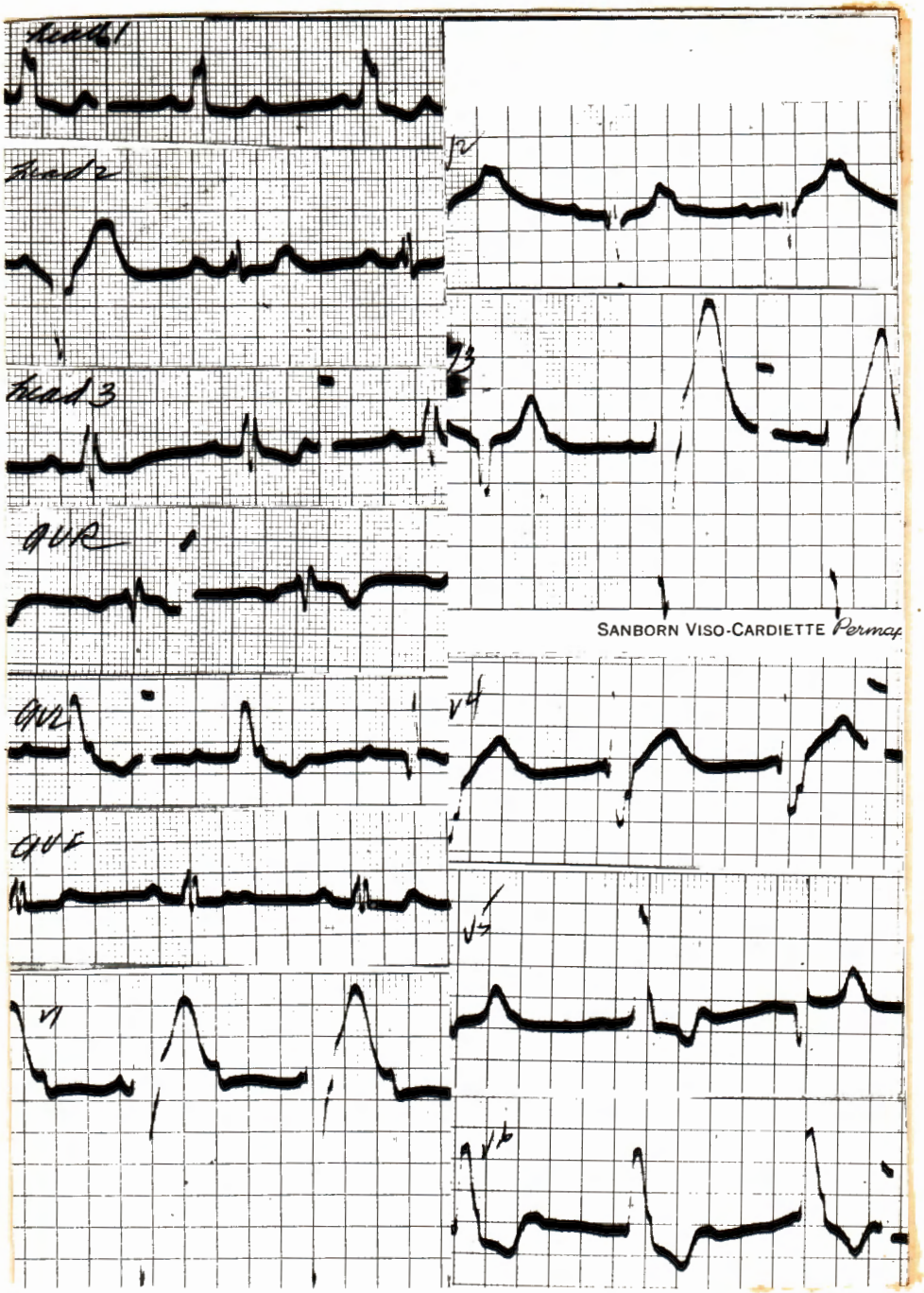

Figure 8. (reduced 11%)

Rhythm: Sinus tachycardia with 2:1 A-V block

Rate: Atrial 112/min.: ventricular 56/min.

P-R: 0.24 sec.

QRS: 0.14 sec.

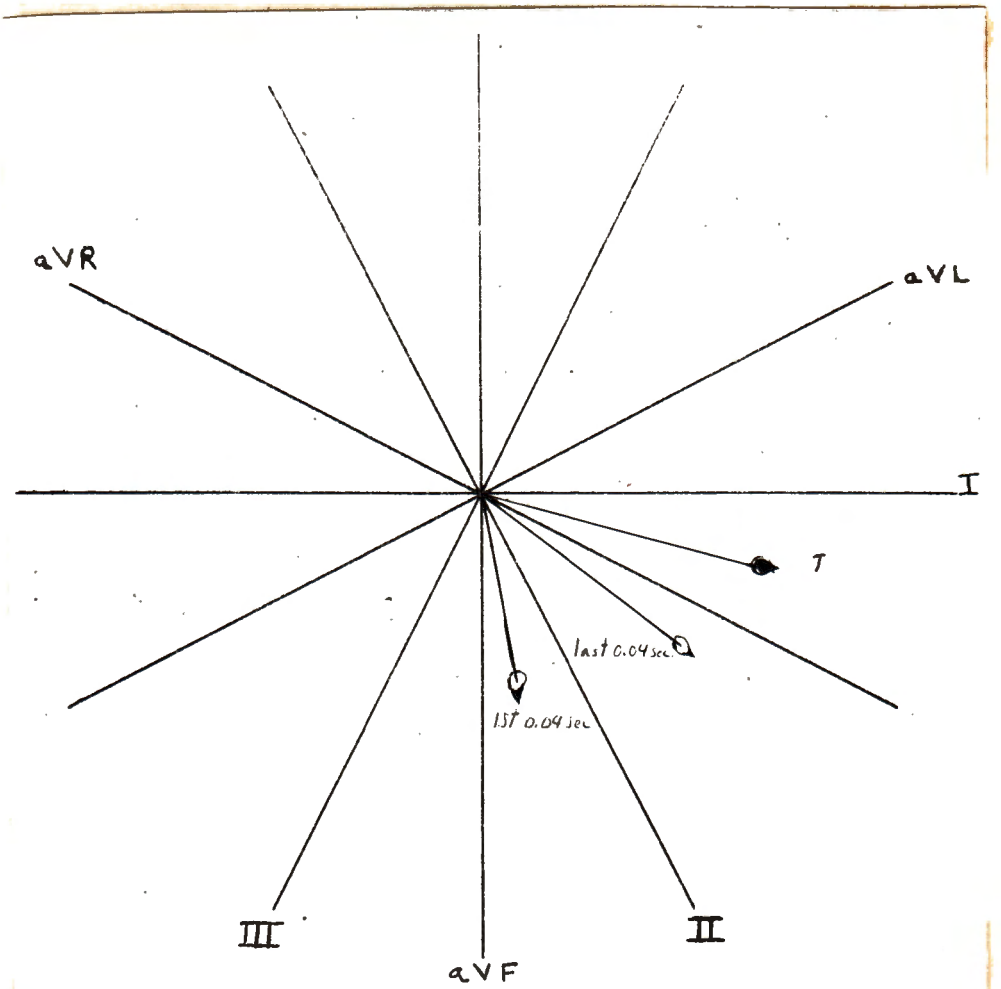

Figure 8-a.

1. Left bundle branch block.
2. Left ventricular hypertrophy.
3. Left atrial hypertrophy (by inspection of P waves)

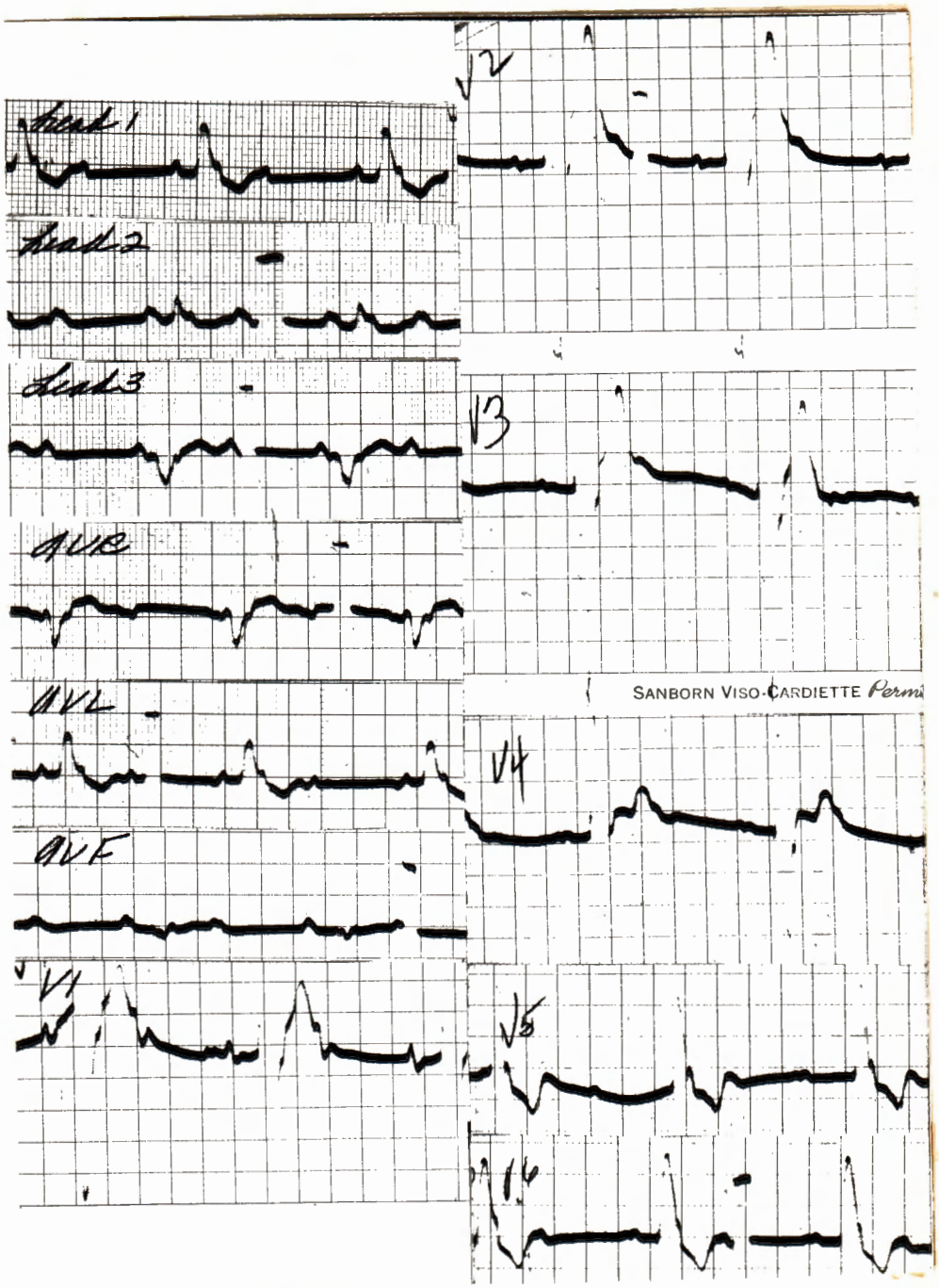

Figure 9. (reduced 11%)

Rhythm: Atrial tachycardia with 2:1 A-V block.

Rate: Atrial rate 106; ventricular rate 53.

P-R: 0.19 sec.

QRS: 0.14

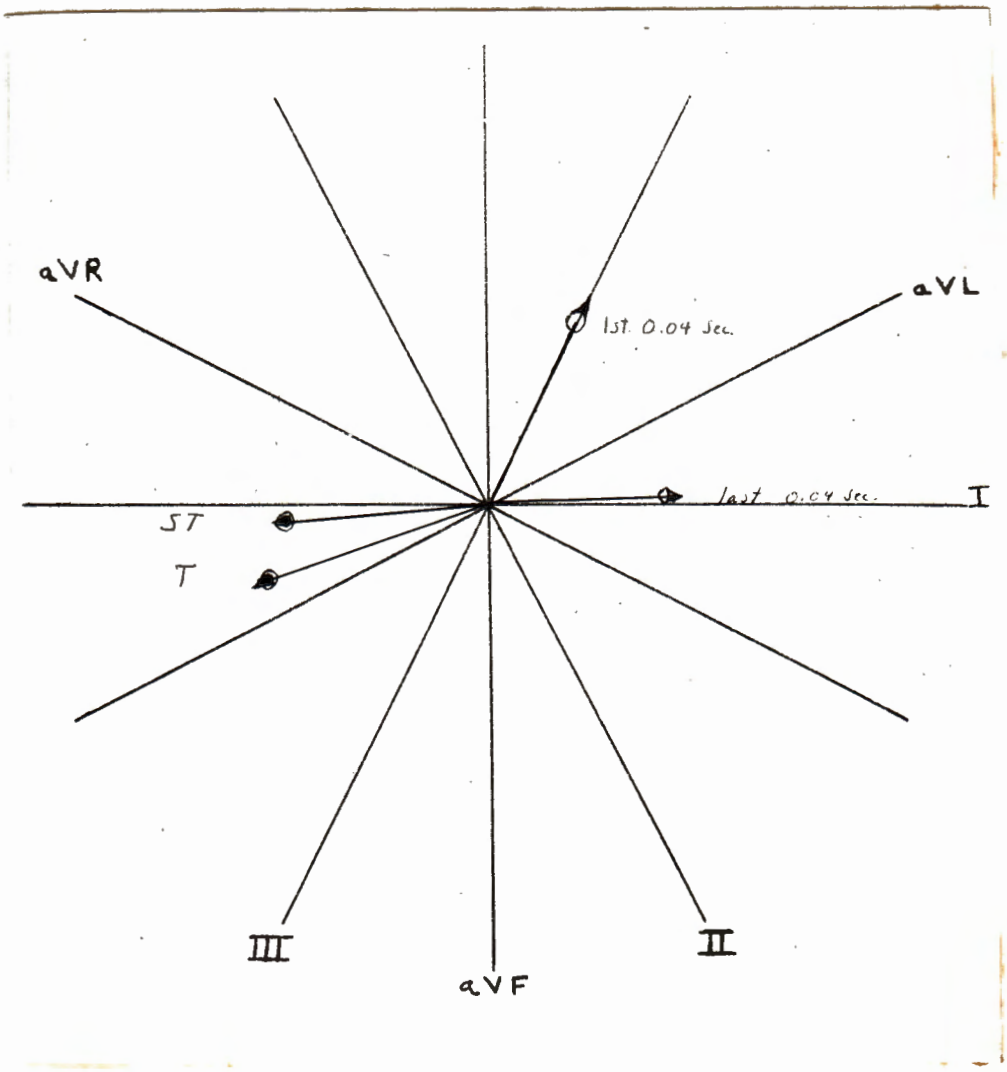

Figure 9-a.

1. Left bundle branch block.
2. Left ventricular hypertrophy.
3. Coronary artery disease.
4. Left atrial hypertrophy (by inspection of P waves).

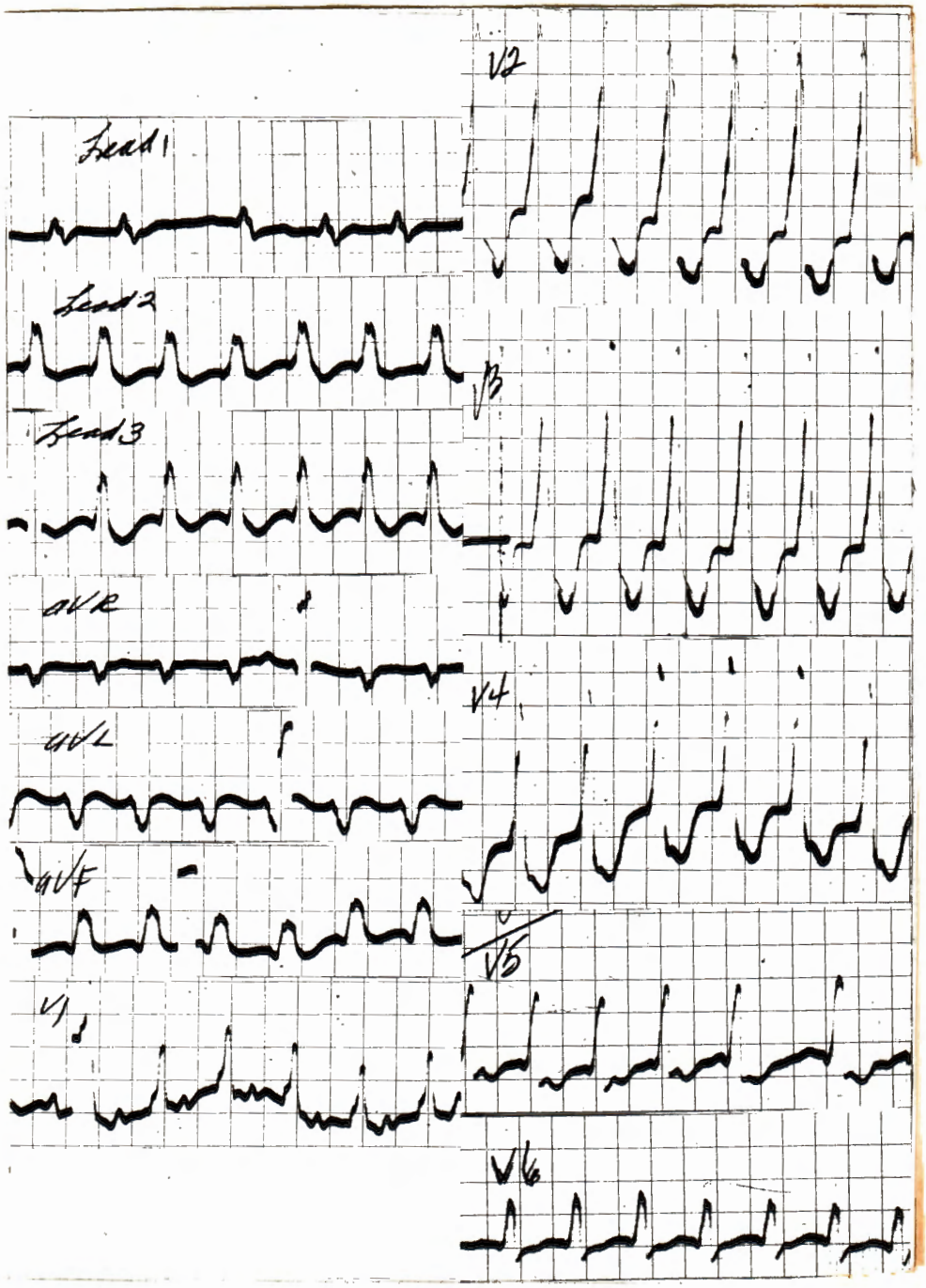

Figure 10. (reduced 7%)

Rhythm: Supraventricular tachycardia; possible Wolf-Parkinson-White syndrome.

Rate: 150/min.

P-R: 0.15 sec.

QRS: 0.12 to 0.14 sec.

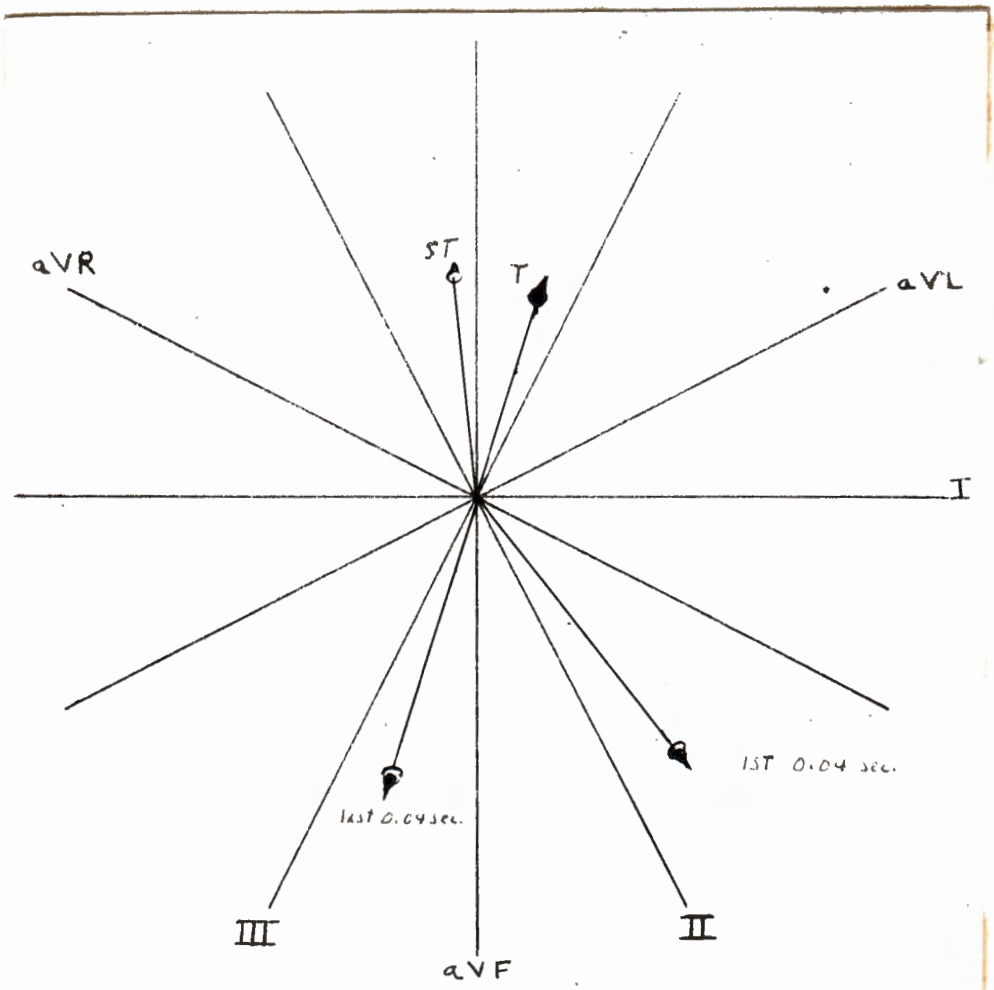

Figure 10-a.

1. Wolf-Parkinson-White syndrome (by inspection of tracing - Delta waves)

2. Ischemia.

3. Possible right bundle branch block.

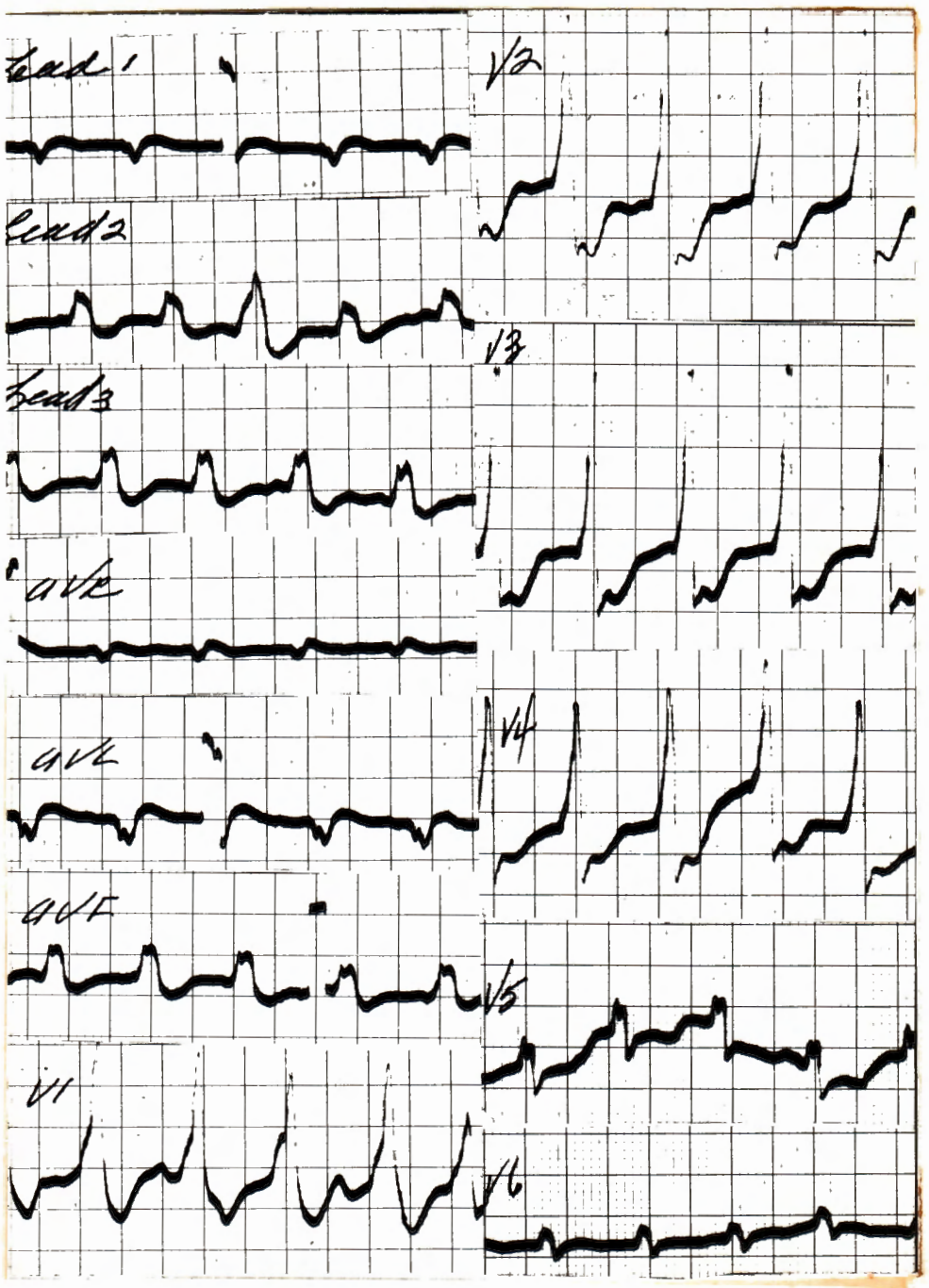

Figure 11. (enlarged 16%)

Rhythm: Wandering pacemaker with tachycardia and Wolf-Parkinson-White Right bundle branch block or ventricular premature beats.

Rate: 130/min.

P-R: Variable

QRS: 0.13 sec.

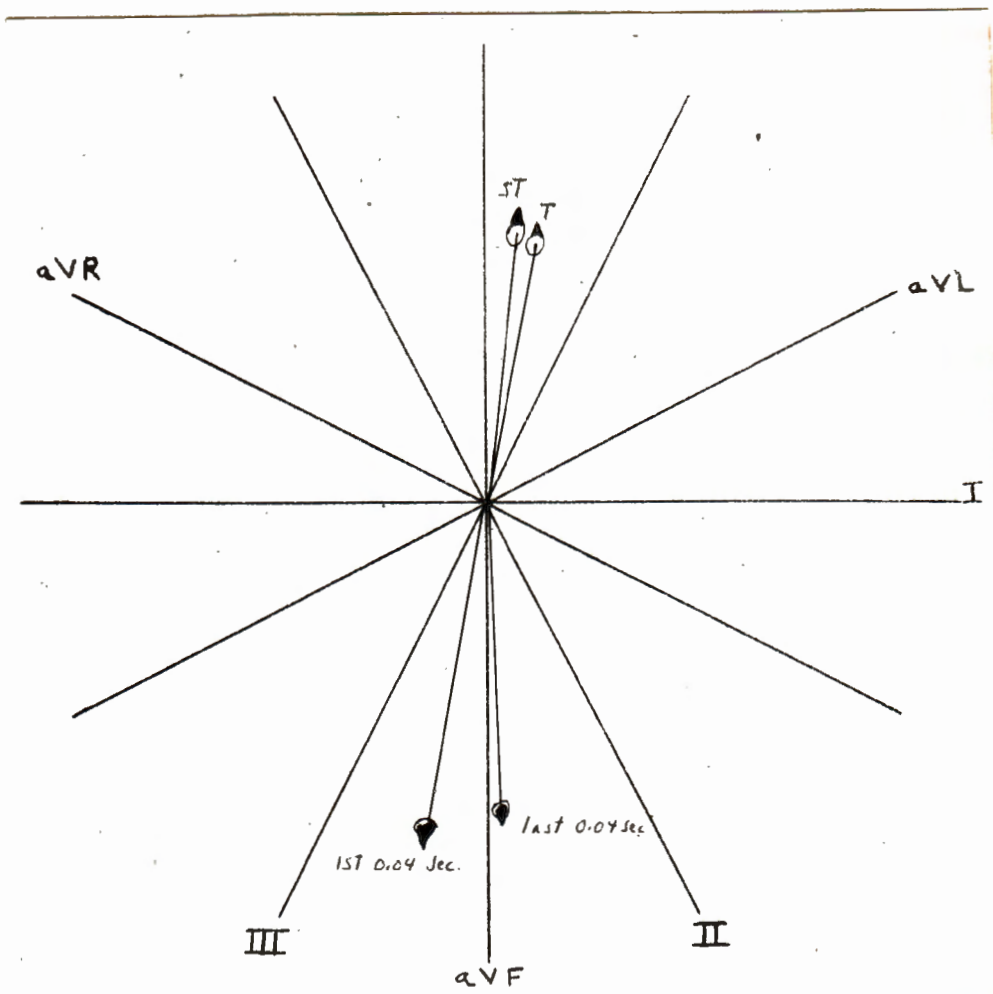

Figure 11-a.

1. Acute posteriolateral myocardial infarction.
2. Ischemia

MECHANISM OF CARDIAC DEATH

Death following occlusion of coronary arteries may result from rupture of the infarcted area (183) or, more commonly, from disturbed coordination of the myocardium so that it no longer pumps effectively. This disturbance begins with chaotic heart action a term which implies the condition in which the normal orderliness of beating and rhythmicity of the heart is replaced by widespread ectopic pacemakers, apparently gaining control of the heart at random. It is obvious that this is but a step to complete incoordination, represented by fibrillation. Death immediately follows the loss of blood to vital centers consequent to loss of the cardiac pump.

Any lesion producing interruption of the normal pattern of myocardial excitation may produce a chaotic rhythm. A convenient division of causes for such an interruption is offered by Hall (184) who considers congenital defects such as septal defects, cysts or aberrant pathways of excitation; inflammatory disease such as diphtheria, staphylococcic myocardial abscess, bacterial endocarditis and syphilis; and vascular lesions such as occlusions of coronary vessels with subsequent infarction or the various causes of ischemia. A further listing includes collagen disease such as rheumatic

carditis, the interference with blood supply seen in the purpuras, drug induced myocarditis, neoplastic invasion and hypertensive changes producing elongation and stretchening of the excitation pathway. (21)

When moribund patients are followed by continuous electrocardiographic recordings during the terminal period (185) cardiac standstill is seen to follow a stage of ventricular fibrillation in about half of the cases, and this occurs regardless of whether the patient dies from primary heart disease or other causes. In those cases when fibrillation does not intervene, heart block at various levels (S-A, A-V, or intraventricular) has developed. The terminal electrocardiograph usually assumes very bizarre patterns with extreme widening and splitting of QRS, marked S-T deviation and tall pointed T waves. Such "agonal complexes" have been recorded up to 45 minutes after death as determined by clinical examination.

SUMMARY AND CONCLUSIONS

George Kennan recently commented that "No work of history ever begins soon enough or ends late enough to be wholly rounded." (195) Such is the case of this review, which is neither confined to one aspect of coronary artery disease nor yet properly surveys its entire scope. An endeavor has been made to introduce the problem of coronary artery disease and comment on the value of the electrocardiogram in the diagnosis of this condition. This is attempted by noting some of the history of coronary sclerosis; its pathogenesis and pathology together with the factors involved in production of the electrocardiographic tracings and the focus which are known to alter such records. A brief comment on the mechanisms of death following infarction of the myocardium is included. Finally are offered a few remarks on the place of the cardiogram in clinical medicine.

Coronary artery disease, which is usually of atherosclerotic origin, has been indicted as causative of an increasingly large number of deaths in America. In 1949, 299,109 deaths were attributed to this disease or its complications. (186) By 1956 this number had increased to 427,516. (187) The importance of an understanding of this disease and the means of its detection

and treatment is apparent to the most casual observer. In considering the several aspects of coronary artery disease noted in this review, one or two points seem to develop.

The chronic nature of the underlying causes of atherosclerotic occlusion of coronary arteries, after perhaps deterring investigations for a time, has invited many studies concerned with the nature of these changes and their possible reversal. Studies thus far have not provided a practical clinical approach except through a diet low in saturated fatty acids, a diet which must be continued throughout life to be really effective. The ultimate answer to control of this disease thus lies in the future.

The second major conclusion is that the electrocardiograph is an imperfect tool in the most skilled hands and should be used only in conjunction with all other information concerning the patient in question. The implications of coronary artery disease are sufficiently grave to demand that the greatest caution be employed in making such a diagnosis. The problem of over-reading or under-reading electrocardiograms is difficult and emphasizes the need to correlate all the information available in concluding a diagnosis by use of the electrocardiogram. Already far too many persons

are limping their apprehensive ways through life, maimed by the unkind cuts of electrocardiographic misinterpretation. Most people do not realize what risks they run when they submit to an electrocardiogram. The value of having a base line tracing for future comparison is not infrequently offset by faulty interpretation of the initial record and the consequent birth of a cardiac neurotic. Frank N. Wilson, the great electrocardiographer, is quoted (188) as expressing the disillusioned regret that most people were in greater danger of having their peace of mind and happiness shattered by an erroneous electrocardiographic interpretation than of being injured by an atomic bomb.

That electrocardiography possesses this capacity for harm is not widely appreciated. It, therefore, is appropriate to recall that influences such as noted above and earlier in this paper may be present in any tracing. To enumerate the causes of this problem is beyond the scope of this review. Be it sufficient to note that a recent article (188) concerning this matter cited nearly 100 situations in which the electrocardiographic pattern can be confused with that of coronary disease.

The electrocardiograph machine is an instrument of considerable precision, but the interpretation of

its precise record is another matter, for the electrocardiogram has a high coefficient of nonspecificity, and it never, alone, proclaims the cause of the disturbance it reveals. The importance of careful consideration of the entire clinical picture before committing one's self (and the patient) to a diagnosis is evident. Only after extracardiac causes of abnormal tracings are eliminated can one conjecture about the cardiac lesion present. A correlation of anatomy, physiology, pharmacology, pathology and electrocardiography is necessary for understanding the patterns seen in clinical medicine.

Interspersed throughout this paper have been comments on the treatment of myocardial infarction. I wish here to briefly summarize the current philosophy of management of this disease, and emphasize the importance of repeated electrocardiographic studies for monitoring of recovery, detection of complications and prognosis.

The management of the patient with acute myocardial infarction is not a standardized or routine procedure, but one which must be carefully individualized within the limits of certain broad principles. The five basic aims of management are 1) establishing the diagnosis, 2) controlling symptoms, 3) preventing and treating complications, 4) encouraging healing and myocardial

revascularization, and 5) supervising post-infarction convalescence and rehabilitation. (189, 190)

A major portion of this paper is devoted to the problem of electrocardiographic diagnosis of infarction. Its use is not limited to diagnosis of the acute episode because, as previously noted, changes which correlate fairly well with anatomic changes can be detailed frequently when one compares tracings obtained as recovery progresses with those recorded early in the course of infarction. Discovery of progressive infarction, aneurysm, ectopic sources of excitation, toxicity from digitalis, quinidine or other drugs and, to some extent, prognosis are among the uses of repeated electrocardiograms. (191)

The remaining items of treatment will not be developed further as they are beyond the scope of this paper. A single comment concerning the future of therapy of infarction will be included. Current interest in the possibilities of surgical reconstruction of occluded coronary arteries (192) is reflected in efforts to develop safe and reliable methods for coronary arteriography. Two recent papers (193, 194) illustrate this endeavor and dramatize the fantastic progress made in diagnosis and treatment of coronary occlusive disease in the first part of this century as compared with the

entire span of recorded history heretofore.

Coronary occlusive disease is, in summary, most commonly atherosclerotic in origin and characterized by both chronic and acute embarrassment of myocardial arterial circulation. If this interruption of blood supply is sufficiently prolonged, infarctions of the heart muscle occur. If the infarcted area be sufficiently large, clinically detectable changes develop among which are alterations in the electrocardiograms. The electrocardiographic tracing, when properly interpreted, frequently provides fairly exact information concerning the age and location of areas of infarction. Pitfalls in such interpretation are many and the careful diagnostician considers the entire clinical picture in concluding the diagnosis of coronary artery disease and myocardial infarction.

Treatment of this problem is unsatisfactory at present but current therapy still has much to offer the patient thus afflicted. The importance of serial electrocardiographic studies lies in the monitoring of myocardial changes made possible by known correlation between histologic and electrocardiographic changes and also in detection of extracardiac abnormalities reflected in the tracing.

Clinical electrocardiography is established as a diagnostic tool and will, in the foreseeable future,

be practiced in the manner currently popular. New methods for electrocardiographic studies are constantly under development but those now extant require a complexity of equipment proportionally far in excess of the additional information which they offer.

ACKNOWLEDGEMENT

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