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Post myocardial infarction syndrome

Richard Bickley Osborne
University of Nebraska Medical Center

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Richard Bickley Osborne

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I. INTRODUCTION

Until recently pericarditis following myocardial infarction has been thought of as an incidental and transient finding in the course of a more important illness (1,2,3,4). Only after the recently published papers of Dressler (5,6,7) was it recognized that in certain cases of myocardial infarction, pericarditis represented a major complication which often overshadowed and outlasted the basic illness, causing in many patients a protracted and sometimes stormy course. This complication of acute myocardial infarction which is similar in many respects to the post commissurotomy syndrome and idiopathic pericarditis was first described by William Dressler in 1955 (1) and consists of a syndrome of fever, chest pain, evidence of pericarditis with or without effusion, pleuritis and pneumonitis and a striking tendency to recur. The condition does not fit any of the usual complications of myocardial infarction listed in the textbooks and it is frequently mistaken for a recurrent myocardial infarction or pulmonary infarction. Larger and growing numbers of patients have been observed with this syndrome since the first paper was presented by W. Dressler in 1955 (8,9,10,11,12,13,14,15,16,17). With the increasing frequency of reports of cases with

similar features, more and more evidence has accumulated to support the validity of this condition. Many cases of pericarditis following myocardial infarction which have been delayed in their appearance or prolonged have not been recognized as a complication in proper perspective until after the reports of Dressler were published (15). Also this condition may be readily overlooked as one does not usually subject a patient with an acute myocardial infarction to frequent and serial roentgengrams of the chest. Confusion or a missed diagnosis can lead to inappropriate therapy and severe or lethal complications in an otherwise benign condition (7). Recognition of this syndrome is not only important for the above reasons but also to the patient and relatives. A correct diagnosis will relieve much mental anguish which usually goes along with the more serious complications of myocardial infarction, namely recurrent or extension of the myocardial infarction and pulmonary infarction. The diagnosis of this syndrome is not difficult to make when the majority of symptoms are present, with the characteristic tendency to recurrence, and the causal relationship to the myocardialinfarction is clear. There are other times when the causal relationship

is obscure because the preceding coronary attack was silent or caused only minor symptoms and there is a lapse of several days or weeks between the onset of the pericarditis and the myocardial infarction. In these cases only will a keen awareness of its occurrence and a high index of suspicion make the diagnosis and reduce the number of cases diagnosed as "idiopathic" pericarditis. Also when patients with unexplained pericarditis, especially those of the older age group, present family histories of diabetes, stroke, hypertension, or arteriosclerotic heart disease, coronary origin of the pericarditis may be suspected (18). The possibility of this syndrome occuring in some arteriosclerotic hearts with large or small areas of ischemic myocardial necrosis without the manifestation of myocardial infarction can be postulated (18, 19). Such an observation may explain the occurrence of unexplained pleural effusions that are sometimes found in elderly and arteriosclerotic individuals who never suffered a clinically observable myocardial infarction (9).

This paper is written as a survey of the accumulative evidence in the current medical literature for this syndrome and to present the diagnostic cri-

teria of the syndrome with some discussion as to the etiology, incidence, course, prognosis, differential diagnosis and treatment with special attention to the danger of anticoagulent therapy in the presence of the post myocardial infarction syndrome.

II. ETIOLOGY

The etiology of this syndrome as in the post-commissurotomy syndrome and idiopathic pericarditis which this syndrome closely mimics is unknown (4,20, 21,22,23,24,25,26). The severity of the infarction does not seem to be a factor, for the complication is observed in both massive and mild infarction. The site of the myocardial infarction, likewise, apparently does not exert a significant influence, for the syndrome is associated with equal numbers of anterior and posterior-wall myocardial infarctions (7).

Many causes for the syndrome have been postulated and will be discussed below.

1. Auto-immune Mechanism. Dressler believes the etiological factor in post myocardial infarction syndrome may represent a reaction to myocardial necrosis with release of autogenous antigens which causes a hypersensitivity reaction in disposed persons (7).

Attempts at culturing bacterial and viral

agents from blood and from pericardial and pleural-aspirated fluid has been unsuccessful nor has it been possible to prove the presence of infection by serologic tests (7,8,10). Antibiotic drugs have been ineffective. A chance coincidence of idiopathetic pericarditis and acute myocardial infarction is unlikely since the incidence of the syndrome complicating myocardial infarction was the same in one series and higher in another series than the incidence of idiopathic pericarditis occuring alone in the general hospital population in the same length of time.(7,8).

It has been shown in both animals and man that allergy might produce pericarditis, pleurisy and pneumonitis (27). The production of antibodies as a defense against foreign protein is a concept which has long been established in medical knowledge and practice. As long as 60 years ago it was shown that antibodies can be produced against ones own tissue (23,29,30). Autoantibody production has been shown to occur against autoantigens produced in the lens, brain, thyroid, adrenal, kidney and skin (28). During the past few years, evidence has accumulated that cardiac tissue can also give rise to the production of autoantibodies (28,31,32). Since the claims of

Masugi and Cavelti (33) there have been a number of reports of the presence of circulating autoantibodies in cases of heart disease, with recent evidence of anti-heart autoantibodies with specificity toward heart tissue (28,29). How this comes about is not clear. It is postulated that there is some change in the antigen pattern of the heart tissue for the body to regard it as "not-self" and produce antibodies against it (28). The concept of an autoimmune reaction as an etiological cause in disease is accepted on a number of characteristics which must necessarily apply to those diseases which are to be explained on an "autoimmune" basis (28). The characteristics are as follows: (1). Symptoms usually appear 2 or 3 weeks following the precipitating event. (2). Reactions are suppressed by corticosteroids. (3). Pathologic lesions show the typical picture of lymphoid granulomatous infiltrations. (4). Evidence of immune reactivity to organ-specific antigens can be found in patients in the form of antibodies in the circulation. (5). Diseases similar in man can be produced in animals by immunization with appropriate organ antigens. (6). Autoimmune disease can be passively transferred by injection of lymphoid cells

from an animal suffering from the disease.

Certain findings in post myocardial infarction syndrome fulfill the above criteria although only partially. Evidence for ascribing this complication of myocardial infarction to an atuoimmunopathologic mechanism is similar to that brought forward in the case of the post commissurotomy syndrome, which it resembles. M. Davies and group have demonstrated the presence of circulating auto antibodies to heart antigens in two cases (28). They have recently demonstrated moderate to high titers of autoantibody in the sera of 3 patients who did not develop the syndrome after myocardial infarction. Gery's group has demonstrated high titers of specific anti-heart autoantibodies in 3 cases of post myocardial infarction syndrome and commented on the striking similarity in the anti-heart antibodies produced by immunized rabbits and by the patients with post myocardial infarction syndrome, suggesting this as support for Dressler's belief (31). They also postulated that the pathogenic autoimmune reation may be due to the action of cell-bound antibodies. Davies group (28) believes there is no direct evidence of a cell-bound antibody in diseases of the heart. Davies, et al,

believe proof of the presence of circulating autoantibodies requires demonstration of their activity against the heart of the individual in question. Both groups suggest that the circulating auto antibodies maybe a consequence rather than a cause of the tissue destruction. In support of the above Lessof (30) postulated recently that autoantibodies might be expected to occur in two circumstances, one in which they play a major role in causing disease, the other in which they develop as a purely secondary phenomenon after a tissue has been injured. So far it is not known whether the autoantibodies that have been reported in human diseases fall into the first or the second category.

No characteristic pathological findings have been observed as yet in the involved pericardiums as described in the criteria for an autoimmune mechanism although there have been a few reports of eosinophilia, eosinophils in the aspirated pericardial and pleural fluid, arthritis, and indolent subcuteneous nodes (6). Steroids have caused dramatic improvement of the symptoms of the syndrome, and in some cases rebound phenomena have occurred with withdrawal of the steroids (7,8,34). In one case repeated recurrences of the

basic disease, persisted for many months and years with repeated withdrawal of steroid therapy making it unlikely that the illness was an infectious process, for it is known that steroids, while suppressing the inflammatory manifestations, facilitate the growth of micro organisms. No evidence of spread of infection was observed in this case (35). The above case lends support to the autoimmune mechanism as the etiological factor in the post myocardial infarction syndrome. In the majority of cases the symptoms were delayed in appearance following the acute myocardial infarction fulfilling another of the criteria for the autoimmune mechanism as an explanation for the cause of this syndrome.

2. Infectious Etiology-Cohen (8) in comparing his series of cases of post myocardial infarction syndrome and Dresslers series thought it a striking feature that the majority of cases in both series occurred within a relatively short period of time. He thought the simple explanation of an increasing recognition of the syndrome, since attention was called to it by Dressler, was inadequate. He also suggested the worthiness of exploring a single etiological factor as the cause of the post myocardial infarction syndrome, the

postcommissurotomy syndrome or postpericardotomy syndrome, and Idiopathic pericarditis since many times the symptoms of the above illnesses are identical. If this be true, it is noteworthy that it has been observed that the postcommissurotomy syndrome seemed to be a frequent complication for a short time, with a high proportion of the operated cases exhibiting it, then for a longer time it was not seen at all (36). This phenomenon is possibily best explained by the sporadic appearance of an infectious agent most likely viral. There also has been an increasing number of reports in which a virus, most often a coxsackie virus, has been the causative agent isolated in Idiopathic pericarditis (8,37). It was pointed out by Cohen (8) that there was a mild epidemic of viral diseases, mostly due to coxsackie, in the summer of 1958 in the hospital area where the cases of post myocardial infarction syndrome were observed. He concluded the high incidence of the syndrome during that period therefore was better explained on the basis of a mild epidemic virus disease than simply the belief that the high incidence was due to an increased awareness of a new syndrome. The suggestions of Faure and others (6)

that myocardial infarction might provide the bases for infection or cause the activation of a latent virus supports Cohen's belief, and with trauma of one kind or another as the initiating factor, the various syndromes with similar manifestations could be brought together. To date though, viral studies on Cohen's cases (8) with special attention paid to isolation of the coxsackie group have failed to reveal any pathogenic agent. This is true also in all other reported cases of post myocardial infarction syndrome. It has been pointed out by Carmichael (38) that a characteristic leukocytosis with left shift, a frequent finding in the post myocardial infarction syndrome, has not been associated in known viral pulmonary or pericardial infections.

3. Anticoagulant Therapy-Anticoagulants have been suspected as the cause of the post myocardial infarction syndrome because of the occasional hemorrhagic manifestation of this syndrome (7,10,27). Goldstein and Wolff (39), reporting on hemopericardium complicating myocardial infarction caused by anticoagulant therapy, stressed the importance of a group of symptoms which, if present, should lead one to suspect hemorrhagic pericarditis. These symptoms are

very similar to those of post myocardial infarction syndrome making it extremely difficult to differentiate between the two conditions. However the hemorrhagic manifestation of the post myocardial infarction syndrome have occurred in patients not receiving anticoagulant therapy and in cases where, although anticoagulant therapy was used, the prothrombin time was in therapeutic range (27).

4. Reaction to blood in the pericardium-Because of the similarity of the findings of post myocardial infarction syndrome and the post pericardiotomy syndrome a common cause for the two syndromes could be postulated. It is believed by Engle (26) and Tabutznik (40) that the pericarditis in the latter syndrome is best described as a reaction to blood in the pericardial sac. Engle's group (26) believe it represents a delayed hypersensitivity phenomenon to the blood in a pericardial sac that has already experienced an immediate traumatic pericarditis following wide incision of the pericardium. Later reccurrences are brought on by less specific stimuli. The condition in their series of cases appeared after pericardial incision, with or without cardiotomy or valvotomy. It has been observed in many patients with congenital

malformations of the heart who survived intra-pericardial surgery as well as in rheumatic patients who recovered from mitral valve surgery. The condition also was observed following exploration of the pericardium for in-operable congenital cardiac lesions. Although other factors may be important in the pathogeneses of this condition, the feature common to all these operations was incision of the pericardium. It may be true that the pericardial reaction which follows myocardial infarction is initially similar to that which results from trauma or incision of the pericardium, the infarction producing the irritation comparable to that of incision or trauma of the pericardium, with leakage of blood into the pericardial sac. Tabutznik's group (40) believe the pericarditis is due to a sterile inflamatory response of the intrathoracic serous membranes to the irritative effects of blood.

III. INCIDENCE

The post myocardial infarction syndrome may be one of the more frequent febrile complications of recent myocardial infarction. It is roughly estimated by Dressler (7) that the syndrome occurs in 3% to 4% of the cases of recent myocardial infarction. It is

difficult to obtain information as to the incidence of the syndrome since the preceding myocardial infarction maybe small with minimal clinical findings or completely unrecognized-"the silent myocardial infarction". In addition the initial episode occurring during hospitalization often remains unrecognized and the second recurrence may not occur until the patient has been discharged from the hospital, with the causul relationship to the basic condition beling lost. Weiser's group (10) believes, in view of the ease with which they collected their cases of this syndrome after becoming aware of it, that this complication may not be uncommon. The Mayo Clinic group (17) believe the syndrome is rare but a constant challenge to decrease the number of cases of acute idiopathic pericarditis. Exact information as to the incidence of the complication will not be available until knowledge of the condition has become more wide spread and the number of reported cases and series in the literature have increased.

IV. SIGNS AND SYMPTOMS

The post myocardial infarction syndrome is characterized by prolonged or recurrent fever, chest pain, and clinical and laboratory evidence of peri-

carditis, pleurisy, and pneumonitis. These abnormalities may occur alone or in combination, and all show a marked tendency to recur. A discussion of the individual signs and symptoms will follow.

1. Pericarditis-Fibrinous pericarditis during the early course of acute myocardial infarction is fairly common, seen in 15% to 32% of patients (7,41, 42). The pericarditis usually appears on the second to fourth day when the evanescent pericardial rub denoting its presence is most commonly heard(43). Pericarditis in patients with the post myocardial infarction syndrome differs in several important respects from that usually associated with infarction. The differential will be discussed later when the differential diagnosis of the syndrome will be presented.

The friction rub which is a significant finding of this syndrome was found in 80% of the cases, developed 3 to 24 days after the infarction and instead of being evanescent, it remained audible 7 to 10 days. Recurrences were common several weeks after the initial episode. Among the 32 patients of Dressler's series (7), 7 cases displayed the friction rub appeared in the second week of illness, 11 in the

third week and 12 later than the third week. In two patients the rub was heard for the first time as late as 10 weeks after the initial episode. In 7 patients the friction rub occurred once or several times during a prolonged illness. In few instances, relapses appeared as late as 2 years after the onset of the illness (44). The rub remained audible for a week or longer in nine patients, for 17 days in two instances and for 3 weeks in one case.

Pericardial effusion, thought to be very rare in myocardial infarction, so rare that it has become the subject of isolated case reports, has been seen in 60% of patients with post myocardial infarction syndrome (1,2,3,9,41,43). Also according to Scott (45), massive effusion with pericarditis resulting from epicardial infarction is uncommon unless, with anticoagulant therapy, bleeding from the infarcted area occurs. In several instances the pericardium was aspirated; the fluid was at times straw colored, and at other times hemorrhagic even in the absence of anticoagulant therapy (7,10,27).

2. Pleuritis-Pleural effusion appearing during the course of myocardial infarction is usually attributed to either congestive heart failure or pulmonary

infarction. It is rare or unknown in uncomplicated myocardial infarction (7,41). In Dressler's series (7) of patients with post myocardial infarction syndrome, pleural effusion was a common finding, appearing in 70% of the cases. In Cohen's series (8) pleural effusion was seen in all his patients. No pleural effusions were observed in Weiser's series (10) of patients with this syndrome. The effusions in the above series and in other isolated case reports was minimal in some, while in others it was of paramount importance necessitating repeated paracentesis for relief. Like the pericardial effusion, the fluid obtained was at times straw colored and at other times intensely hemorrhagic (6). In Dressler's series (7) the pleural effusion was unilateral in 8 and bilateral in 16 patients.

It is interesting to mention that Ellis and McKinley (46) and McKinley (47) have reported on pericarditis and pleurisy in patients developing they believe from a hypersensitivity reaction to different agents.

3. Pneumonitis-Pneumonitis develops in approximately 25%-30% of patients with this syndrome occuring less frequently than pericarditis and pleurisy (7).

Cohen (8) believes pneumonitis is possibily an uncommon finding here. Onset of the pneumonitis is characterized by dyspnea, basal rales, and cough in the absence of congestive heart failure. Occasionally hemorrhagic expectoration occurs. X-rays have shown evidence of pulmonary infiltration, either linear or in patches, mostly located in the bases of the lungs. In none of the cases so far reported have the pulmonary changes been associated with thrombophlebitis, pulmonary embolism, or congestive heart failure. In one case of Dressler's series a rapidly spreading bilateral pulmonary infiltrate treated with prednisone was followed by rapid improvement while the progress was not influenced by antibiotics. Geever (48) has reported on 3 cases of hemorrhagic pneumonia after myocardial infarction with microscopic features similar to those found in atypical pulmonary inflammatory reactions. The one case of Dressler's series that had postmortem examination did not show the specific features described by Geever (7).

Rich and Gregory (49), Ellis and McKinley (46), and Harkary (50) have reported cases of pneumonitis with findings of an atypical pulmonary reaction associated with pericarditis and pleurisy which they be-

lieved were caused by an allergic or hypersensitivity reaction to certain unrelated agents. The inflammatory complications of acute myocardial infarction, including those of a hemorrhagic nature, may likewise be allergic in nature.

4. Hemorrhagic exudate-A tendency to hemorrhagic inflammation should be included as one of the characteristics of post myocardial infarction syndrome (7,10,27,34,51). Intensely hemorrhagic exudate has been observed in reported cases of this syndrome in the absence of anticoagulant therapy or with the prothrombin time within normal limits when anticoagulant drugs were being used (27). This fact should be emphasized because of the great tendency to attribute hemorrhagic complications of myocardial infarction to the use of anticoagulants. Many cases of hemopericardium complicating myocardial infarction fit the clinical picture of the post myocardial infarction syndrome. Much of this confusion is due to the close adherence of Goldsteins criteria for hemorrhagic pericarditis (27,39). The danger of pericardial bleeding and cardiac tamponade in patients with generalized pericarditis who receive anticoagulant therapy should not be underestimated. The one

death in Dressler's series (7) was caused by hemorrhagic cardiac tamponade in a patient receiving anticoagulant therapy. Hemorrhagic pneumonitis developing after myocardial infarction is easily diagnosed as pulmonary infarction.

5. Chest Pain-Beside fever, chest pain of a pleuropericardial character or less often, of an anginal type is the most common symptom and the most sensitive index of the complicating pleuropericarditis (6,7). It often precedes the onset of the fever but usually appears at the time the temperature becomes elevated. In exceptional cases, the pain may be absent throughout the entire course of the illness (10). Sometimes missing in the first attack it may appear with the second or third flare-up. The pain is described by different patients as a "pressing, squeezing, tightening, searing, sharp, stabbing, or sticking" sensation. In milder cases the pain is described as a "dull, pulling or drawing sensation". The intensity varies widely from a crushing and agonizing pain to a dull or raw feeling which patients may fail to mention unless questioned or asked to take a deep breath. An all important characteristic is that the pain is aggravated by deep inspiration, turning in

bed, yawning, coughing or in rare instances swallowing. The site of the pain may also vary, but is usually present in the chest most noticeable in the substernal area and precordium. Other sites include both sides of the neck, jaws, shoulders, arms, the supra clavicular areas, the epigastrium, and the hypochondrium. Often the pain caused by deep breathing is located exactly in the area where the pericardial friction rub is audible. The pain may last a few hours or several weeks with varying intensity. The substernal location, elicited by or aggravated by deep inspiration, appears to be one of the most characteristic marks of pericarditis.

6. Fever-Fever which is usually present in the syndrome is variable in degree and duration. The average range is 100'-103' F with occasional peaks to 103' and 104' F. The fever may last one day or up to one month. The fever of the syndrome when coinciding with the initial febrile period of the myocardial infarction may be ill-defined or may cause a second peak or a plateau type of temperature curve which is higher than that of uncomplicated myocardial infarction, and cause prolongation of the initial febrile period (6,7,10). Between flare-ups of pleuro-

pericarditis when the process is smoldering, the temperature may drop to around 100' F with secondary rises with relapses of the pericarditis. In some patients the temperature never runs higher than 100' F in spite of the presence of generalized pericarditis. Post myocardial infarction syndrome should always be considered in the differential when a patient convalescing from a myocardial infarction begins running a temperature (13).

V. LABORATORY

1. Laboratory-Laboratory findings are not considered to provide much information of diagnostic importance although Dressler believes a persistent leukocytosis and an elevated sedimentation rate suggest continual activity of the process even when a drop in temperature seems to indicate a return to normal (8,8). Leukocytosis of 10,000 to 20,000 per cubic millimeter, occasionally elevations to 35,000 per cubic millimeter, with a relative neutrocytosis, and left shift is present in the vast majority of cases. Eosinophilia was observed in one-fifth of Dressler's cases (7). In contrast to the short duration leukocytosis in recent uncomplicated myocardial infarction, the leukocytosis of the complication may

persist for weeks. The persistent elevation of the sedimentation rate seen almost in all of the cases is considered a nonspecific reaction to necrosis (8). The slight increase in transaminase activity in some cases after the initial peak elevation due to myocardial infarction is consistent with superficial myocardial involvement seen in pericarditis (8). Correlation with clinical findings is necessary to exclude any extension of the infarction, or development of a new one (10). In cases of the complication with a protracted course or with hemorrhagic manifestations the hemoglobin may drop, necessitating in exceptional cases the transfusion of blood. Furthermore, in protracted cases, hypoproteinemia occasionally develops. In Jones' (13) reported case of the complication there was elevation of the globulin with the suggestion that the globulin rise had occurred in the alpha 2 and gamma fraction on the basis of serum electrophoretic studies. This group did not believe the serumprotein changes were striking enough to be considered as diagnostically or etiologically significant. Cultures of blood and pericardial and pleural fluid have not yielded growth in any of the reported cases of this syndrome. Search for acid-fast bacilli,

tests for lupus erythematosus cells, cold agglutinins, heterophile antibodies, agglutinins for typhoid, paratyphoid, and brucella, and tuberculin tests have also been negative in all of the reported cases of post myocardial infarction syndrome.

2. Electrocardiogram-Electrocardiogram is of only limited value for the diagnosis of pericarditis when recent myocardial infarction is present and the electrocardiographic diagnosis of pericarditis may be difficult or impossible in this situation (7,17). The criteria for the electrocardiographic diagnosis of pericarditis which complicates myocardial infarction was first established by Barnes (52) and extended by Langendorf (53). Further discussion can be found in the reports of McGuire (14), Likoff (17), and Hull (54). Barnes (52) pointed out that the reciprocal relationships between the RS-T segments in the bipolar leads I and III are replaced by an uniform elevation or upward rounding of the RS-T segments in all the bipolar leads. This may later be followed by inversion of the T-waves in all bipolar leads. Langendorf (53) stressed the importance that both QRS and S-T-T changes in the limb and chest leads have to be taken into account and studied in their

relation to each other, if uncomplicated diffuse pericarditis is to be differentiated electrocardiographically from myocardial infarction and from myocardial infarction complicated by diffuse pericarditis. He also stresses the importance of serial electrocardiograms during the S-T stage of infarction to increase the number of correst diagnoses of pericarditis complicating a recent myocardial infarction. Evans (25) has reported that EKG findings will vary from patient to patient and in some patients from time to time depending on the amount of involvement; another reason necessitating repeated examinations to make the correct diagnosis. On many occasions the EKG will be atypical or show only part of the typical pattern (54).

In some cases, but not in all, when pericardial effusion is associated with the pericarditis the amplitudes of all waves and complexes in extremity leads are diminished, but such diminution is most likely to occur in precordial leads (54). In a considerable number of effusions, even large ones, amplitudes are not abnormally small. In Dressler's series (7) changes of the electrocardiogram compatible with pericarditis was observed in one-half of the patients in whom adequate electrocardiographic studies

were available. 3 out of the 10 cases reported by Cohen showed electrocardiographic evidence of pericarditis complicating the myocardial infarction. The best electrocardiograms can do is strongly suggest the presence of pericarditis but only rarely, if ever, are they in themselves diagnostic.

3. Roentgenography-Roentgenography contributes significantly to the diagnosis of the post myocardial infarction syndrome. X-ray evidence of pericardial effusion, pleural effusion, and pneumonitis has been noted in combination or singly in almost all the reported cases of the syndrome in which adequate studies were made (7,8). According to Dressler (7) serial X-ray studies in addition to thorough clinical observation, are of greatest importance in the recognition of the post myocardial infarction syndrome. Pericardial effusion is often not recognized, because patients with recent myocardial infarction are not usually subjected to X-ray study; If they are, a moderate amount of effusion is interpreted as enlargement of the heart unless serial studies are done (7, 14,55). The necessity of serial X-ray studies was stressed by all authors. The most valuable X-ray evidence of pericardial effusion is a rapidly enlarg-

ing, poorly pulsating cardiac silhouette followed by rapid shrinkage of the cardiac shadow. Another valuable clue is the loss of the retrosternal clear space in the absence of former evidence of enlargement of the out flow tract of the right ventricle in congenital or rheumatic heart disease. At times, radiologically speaking, distinction from cardiac dilatation due to myocardial infarction is very difficult (14). In both conditions, unfortunately, the chest film may be entirely normal or the typical X-ray changes in heart configuration will not be observed. However, even in the above instances roentgengraphic study may still be helpful. A localized pulmonary infiltrate is sometimes associated with post myocardial infarction syndrome, whereas widespread pulmonary congestion and edema is most indicative of cardiac failure following myocardial infarction. The cardiopericardial silhouette may rapidly enlarge soon after the onset of either condition, but it occurs more frequently and to a greater degree in the post myocardial infarction syndrome. Fluoroscopically, impairment of pulsation is more generalized in the complication than the localized pulsation impairment or even paradoxical pulsation seen in cardiac dilatation following

myocardial infarction (14,55). Angiocardiography could be very helpful in difficult differential problems (14,55). Dye filled chambers of the heart well within the shadow of the cardiac silhouette is very suggestive of pericardial effusion. For further discussion see report of Steinberg (55).

VI. DIAGNOSIS

Diagnosis of post myocardial infarction can be made only if the condition is borne in mind. Recognition is not difficult if one is aware of its occurrence and the patient presents with the full-blown clinical picture. In its less classical form, when only the incomplete syndrome appears, it should be suspected, especially if there are recurrences. It may also be suspected when, after acute myocardial infarction, the fever does not return to normal at the end of the first week and no other cause can be established, or when a rise in temperature occurs after the initial febrile period accompanied by pain of the pleuropericardial type. The diagnosis can be confirmed when there are additional signs such as a pericardial friction rub especially when it is of unusually long duration, electrocardiographic and roentgenographic evidence of pericarditis, signs of pleural or pul-

monary involvement, and a tendency to recurrences. The diagnosis becomes difficult when fever is the only manifestation or when pneumonitis or pleural effusion is the dominant feature. The diagnosis may be readily missed if the manifestations of the myocardial infarction are so mild or atypical as to remain unrecognized, and therefore not obviously related to an attack of pleuropericarditis and fever, which appears several weeks later.

Recognition of the syndrome is important in regard to anticoagulant therapy (7). Anticoagulant therapy, which is used when extension of myocardial infarction or pulmonary infarction is diagnosed, is dangerous and contraindicated, unless the patient is under careful observation, in the presence of generalized pericarditis (34).

VII. DIFFERENTIAL DIAGNOSIS

As mentioned above the manifestations of the complication can be readily misinterpreted or missed altogether, although, usually the post myocardial infarction syndrome constitutes an entity sufficiently distinct that confusion with other disorders need not arise. The main or most common illnesses that can be confused with the post myocardial infarction syndrome

are the following:

1. Recurrent Myocardial Infarction
2. Pericarditis Epistenocardia
3. Pulmonary Embolism
4. Congestive Heart Failure
5. Pulmonary Infarction
6. Hemorrhagic Complications of Anticoagulant Therapy
7. Dissecting Aortic Aneurysm
8. Idiopathic Pericarditis

The temporal relationship to myocardialinfarction is of course the chief feature for orientation.

1. Recurrent Myocardial Infarction-Recurrent chest pain and fever following acute myocardial infarction are often mistaken for extension or recurrence of the infarction. The following points are important when considering this differential.

A. When previous EKG's clearly indicates massive myocardial infarction prolonged or recurrent chest pain is rarely caused by extension of the infarction, but more commonly caused by pericarditis.

B. Chest pain aggravated by breathing and change in position is very suggestive of Pericarditis associated with the syndrome and not of myocardial infarction.

C. Anginal pain is very rarely observed in the post myocardial infarction syndrome.

D. A negative electrocardiogram for evidence of extension or recurrence of myocardial infarction helps to rule it out.

E. In the absence of heart failure pleuritis is not a complication of myocardial infarction (43).

F. Absence of radiographic evidence of involvement at the left lung base helps to rule out acute myocardial infarction (43).

2. Pericarditis Epistenocardia-Pericarditis epistenocardia is an insignificant finding involving the pericardium which accompanies recent myocardial infarction (41). Many authors agree that this pericarditis is transient and incidental (1,2,3,6,11,14, 41,42) usually localized but occasionally diffuse. The occurrence of this minor complication following acute myocardial infarction is between 15-32% with its sole clinical manifestation being a fleeting pericardial friction rub (1,2,3,41,42). In Stewart's series (42) of 60 cases of coronary thrombosis with myocardial infarction examined at necropsy pericardial involvement was found in 48 (80%). Of these a transient friction rub was heard in 8 (13%).

Pericardial effusion is considered by all to be a rare occurrence in myocardial infarction and is the subject for isolated reports in the literature (1,2, 6,7,11,14,41,42). Levy (56) has never observed pericardial effusion in detectable amount when associated with the pericarditis of myocardial infarction. The main differential points are the following:

A. The pericardial friction rub is usually heard in pericarditis epistenocardia between the 2nd and 4th days of the illness less frequently hours after the myocardial infarct and very rarely may not occur until 5-10 days after the infarction.

B. Pericardial friction rub of this minor complication is characteristically fleeting lasting a few hours to a few days, rarely may it persist for 1 week.

C. Pericardial effusion is extremely rare in pericarditis epistenocardia and not associated with pleuritis and pneumonitis.

D. Finally the pericarditis of this more minor manifestation of myocardial infarction does not recur.

3. Pulmonary Embolism-When there is chest pain of

a pleuropericardial type present with pleural effusion and pneumonitis and especially when there is hemoptysis or hemorrhagic pleural fluid it is difficult to exclude the diagnosis of pulmonary infarction. The following may be helpful in the differential:

A. Evidence of pericarditis and or pericardial effusion is not usually a feature of pulmonary infarction but is common in the post myocardial infarction syndrome.

B. Absence of the characteristic X-ray signs of pulmonary infarction help to reject it although it is recognized that emboli to this organ need not give any signs or symptoms.

C. Absence of hemorrhagic sputum and signs of peripheral phlebothrombosis are arguments against the diagnosis of pulmonary infarction.

D. Little or no pleural effusion is present in pulmonary infarction.

E. The peculiar temperature curve of the post-myocardial infarction syndrome with protracted periods of low grade fever between high peaks of temperatures associated with flare up of pain is against the

diagnosis of pulmonary infarction.

F. Finally the total clinical picture and a uniformly favorable out come would appear to provide adequate grounds for rejecting the diagnosis of pulmonary infarction.

4. Congestive Heart Failure-The finding of an enlarged heart with pleural and pneumonic involvement may on occasion lead to the erroneous diagnosis of congestive heart failure and dilatation of the heart unless serial X-rays of the chest are taken to show a rapidly shrinking heart (14,54).

5. Pulmonary Infection-At times, with the presence of pleuropericardial pain and pneumonitis, it may be difficult to exclude a pulmonary infection (8). The absence of sputum, the failure to isolate organism, the lack of improvement with antibiotic therapy, and the favorable clinical course with or without the use of steroids help to rule out the possibility of a pulmonary infection.

6. Hemorrhagic Complications of Anticoagulant Therapy-The differentiation of the syndrome from hemorrhagic pericarditis due to anticoagulant therapy may at times be extremely difficult, especially when the hemorrhagic manifestations of the syndrome are present.

Close adherence to Goldstein and Wolf's criteria for hemorrhagic pericarditis will only compound the difficulty (39). The absence of dangerously high levels of the prothrombin time with no evidence of hemorrhage in other organs should help rule out this complication of anticoagulant therapy.

7. Dissecting Aortic Aneurysm-Since a dissecting aortic aneurysm can mimic closely the symptoms of the post myocardial infarction syndrome it should be mentioned in the differential diagnosis (43). The characteristic signs and symptoms of the dissecting aortic aneurysm should not make the differentiation difficult and the pleural effusion when it occurs in this illness is usually unilateral, hemorrhagic, and occupies the left hemithorax.

8. Idiopathic Pericarditis-The signs and symptoms of post myocardial infarction syndrome are identical to those of idiopathic pericarditis and a common etiological factor may be operating in both (4,15, 20,21,55). The temporal relationship to the preceding myocardial infarction is the big differential point. Other causes of pericarditis should also be eliminated before the diagnosis of the post myocardial infarction syndrome is made (14).

VIII. COURSE

The clinical course of the post myocardial infarction syndrome is variable and one symptom may dominate the clinical picture, but the central theme of serositis is apparent in all cases. It is on occasion difficult to determine the onset of the complication but in most cases, especially when the majority of the characteristics are present, early development of the complication is easily determined. A pericardial friction rub, fever, and pleuropericardial pain are the usual characteristic signs noted in the first week of illness. The initial febrile period usually lasts longer than in uncomplicated myocardial infarction and the temperature is usually higher and often marked by a second peak of fever when the complication is present. Whenpneumonitis is present it is also seen in the first week of the illness. Pericardial or pleural effusion, however, is infrequently noted before the beginning of the 3rd week and in occasional instances not noted until the 10th or 115th week of illness. Individual episodes of chest pain and fever usually last for a week or two; uncommonly, from three to six weeks.

The primary significant feature of the syndrome is

its great tendency to recurrence. The number of recurrences range from 2 or 3 episodes up to 4 or 7 bouts and there is one reported case of 8 seperate attacks. Between flare ups the temperature may return to normal but persistent leukocytosis and an elevated sedimentation rate should indicate to the careful observer that a stage of smoldering activity exists. The duration of the complication depends on the number of recurrences. The total duration varies from 7 to 10 days, to as many weeks with occasional cases persisting for 6 to 9 to 10 months and reported rare cases lasting up to 24 months and 28 months respectively (7). Steroid therapy, with relapses following withdrawal of the medication, seems to be the cause of most of the very prolonged cases (34, 35). However, the one reported case lasting 28 months did not receive steroid therapy until the last episode occurred (44). Antibiotics did not alter the clinical course in any of the cases where they were used.

IX. TREATMENT

Treatmentof the post myocardial infarction syndrome depends on the severity of its manifestation (34). Since the condition is self-limited, it may not require any treatment, especially when fever and

pain are slight or absent (7,8,10). Large exudates are sometimes spontaneously absorbed at a rapid rate even in the absence of therapy. Most important, then, is early recognition of the complication to counteract the anxiety of the patient and relatives who may believe either another myocardial infarction has occurred or a pulmonary infarction has developed.

Relief of pain is needed in most instances of the syndrome in which discomfort in the shoulders and chest is a prominent symptom, varying in intensity from a dull ache to a crushing pain. The use of aspirin and codeine may be all that is needed in a few instances. In the majority of cases, though, administration of demerol or morphine is necessary. When chest pain persists and remains severe use of the corticosteroids is indicated. Although salicylates are considered only as analgesics for chest pain in this syndrome Jones (13) found in his case that large doses of salicylates are of therapeutic value in the over all management of the complication and suggests their clinical trial when steroids are contraindicated.

Corticosteroids have a very gratifying and dramatic effect and seem to be almost specific for the condition, relieving symptoms in 24 hours (7,8,9,10,

12,34). Because of the beneficial, dramatic effect of the steroids the temptation to use them as soon as the diagnosis of the syndrome is made is very great. However, in many instances repeated relapses have occurred with the withdrawal of the steroids necessitating the resumption of hormonal therapy and with the resultant prolongation of the illness (34, 35). In one patient flare-ups of the syndrome were observed after one and two years, respectively, of continued steroid therapy following withdrawal of the drug (35). In other instances withdrawal of steroids was followed by nausea, fall in arterial pressure, and cessation of urine secretion. In one case withdrawal of steroid therapy was followed by manifestations of adrenal insufficiency (34). Therefore, it is recommended that steroid therapy be used in only those cases where the course of illness is unduly prolonged, or the illness is severe due either to intractable pain and high temperature that cannot be relieved by any other means, or there is an extensive, rapidly spreading pneumonitis (7). In the above instances steroid therapy brings about a prompt and satisfying resolution of the symptoms. When steroids are indicated and prednisone is used the initial

daily dosage varies from 40-60mg. depending on the severity of the complication. The dose is slowly reduced to zero within a period of four weeks. Reduction and withdrawal of the steroids, in the majority of cases, results in recurrence of the syndrome. This usually necessitates the resumption of hormonal therapy, starting with a daily dose of 20 or 15 mg. After a week or two the steroids may be withdrawn in many instances without ill effect. However, in about 20 per cent of those patients receiving hormonal therapy repeated relapses occur, whenever the steroids are withdrawn, necessitating continuation of the therapy.

Paracentesis of pleural effusion is indicated when the effusion is large enough to cause difficulties in breathing. In the majority of cases, however, effusions in the pleural cavities are of small or moderate size, and capable of complete absorption within a period of one or two weeks.

When pericardial effusion is large causing circulatory embarassment and there is no tendency toward spontaneous absorption of the exudate, aspiration by paraentesis is advisable. Withdrawal of even a few millileters is sometimes followed by rapid

absorption of the exudate. Also the finding of bloody fluid in the pericardial sac serves as a warning in those instances where anticoagulant therapy is contemplated.

Anti-coagulant Therapy in the presence of generalized pericarditis is dangerous and contraindicated unless the patient is hospitalized in an institution in which all safeguards for early recognition and treatment of cardiac tamponade are present (34). When the above requirements are fulfilled, administration of anticoagulants may be continued using special care to avoid dangerously low levels of prothrombin. Frequent checks must be made of the urine for the microscopic appearance of blood, and of the blood for sudden reduction of the hemoglobin value. The one fatal case in Dressler's series (7) was due to cardiac tamponade in a patient with pericarditis receiving anticoagulant therapy. Cohen (8) agrees that withdrawal of anticoagulants is indicated in the presence of pericarditis in most, if not in all, instances. He suggests, however, that the fact that they did not encounter any difficulties when they persisted in the use of anticoagulants, might be an important consideration in cases where the necessity

for their use might be over-whelming.

It is suggested the patient may be allowed out of bed after recovery from the syndrome in about one week or ten days, provided that the basic myocardial damage does not contradict this (7).

X. PROGNOSIS

The prognosis in a patient with the post myocardial infarction syndrome seems to differ little from that of the underlying infarction except for pericardial hemorrhage which is a danger if anticoagulants are not withheld when pericarditis appears (7). In Dressler's series (7) the outcome was favorable in all the patients except the one patient erroneously treated with anticoagulants. The syndrome is important to recognize because of this essential benignity and good prognosis, although the illness if oftened recurrent and sometimes of long duration.

XI. SUMMARY

This has been a survey of the literature of an unusual complication of myocardial infarction characterized by pericarditis with or without effusion, fever, pleuropericardial pain, pleuritis and sometimes pneumonitis occurring at varying intervals after the infarction and with a striking tendency to recurrences. It

is also suggested that the syndrome may require extension toinclude those patients which present with idiopathic pericarditis and history of myocardial fibrosis on an arteriosclerotic basis.

The etiological factors in the syndrome were discussed in some length with special emphasis on an autoimmune mechanism as the most probable explanation for the syndrome. The complication fulfills most of the criteria necessary to place it in the group of illnesses postulated to result from an autoimmune reaction. Further work needs to be done to provide additional proof of such an etiology. No studies have been made to observe the activity of the heart autoantibodies on the heart of an individual involved. Also it has been suggested that the circulating autoantibodies found in a patient with this disease may be the consequence rather than the cause of the tissue destruction. Lack of positive bacteriological studies seems to dispute the infectious process as the etiological factor in this complication. The common observation of this syndrome in patients not receiving anticoagulant therapy and in others where the prothrombin time was within therapuetic ranges when anticoagulant drugs were used is strong evidence

against the hemorrhagic complication of anticoagulant therapy being the etiological factor. The possibility that this syndrome may be a reaction to blood in the pericardial sac can not be excluded at this time. Also mention was made of the similarity of this syndrome to the postcardiotomy syndrome and idiopathic pericarditis with the suggestion that they all may have a common etiological bases.

The incidence is believed to be between 3 and4% but additional and bigger series must be reported on before a statistical validpercentage can be reliabily reported.

The signs and symptoms were discussed in detail with some emphasis placed on the hemorrhagic features seen in many of the reported cases with the proper conclusion to give them a prominent place in the characteristic manifestations of the syndrome.

Of the laboratory and special studies it is felt that serial X-rays of the chest are the most valuable aids in diagnosis. EKG's while helpful for the differential diagnosis are of limited value in diagnosis of pericarditis following myocardial infarction. The various determinations including white blood cell counts, sedimentation rate, and serum transaminase

values are of limited use except to indicate smoldering activity.

Discussion of the differential diagnosis quite clearly pointed out the differences between this major complication of myocardial infarction and pericarditis epistenocardia. Other important illnesses that may be mistaken for this syndrome with possible catastrophic consequences in regard to therapy include recurrent myocardial infarction, and pulmonary embolism. The lack of EKG evidence of recurrent infarction, and the characteristic pleuropericardial pain help to eliminate the former. The lack of radiographic evidence of pulmonary embolism, plus the lack of evidence of hemorrhagic expectoration and peripheral plebothrombosis argues against the presence of the latter. Finally the total clinical picture, the tendency to recurrences and an iniformly favorable outcome would appear to provide adequate grounds for rejecting the diagnosis of the two conditions.

The course of the disease is variable with the characteristic symptoms appearing usually in the first week of illness. The striking tendency to recurrences is seen in most cases with the number of episodes ranging between 2 and 7 with in-between periods of

apparent good health or smoldering activity. The individual episodes last usually one or two weeks. The total duration of the illness varies between 7 days and 28 months and is entirely dependent on the number of recurrences.

Steroids are specific for the management of the illnesses causing dramatic relief in 24 hours. But, because of the many complications of steroid therapy and the common observation of relapses following their withdrawal, prolonging the duration of illness, their use should be reserved for severe, protracted cases, when pain cannot be controlled by other means or when there is rapidly spreading pneumonitis. Symptomatic treatment for relief of pain is all that is needed in most cases. Paracentesis of pleural and pericardial exudates is indicated when necessary. Anticoagulant therapy is contraindicated in all cases of generalized pericarditis unless there are safeguards for early recognition and treatment of cardiac tamponade.

Prognosis is very favorable in this illness which is considered a benign condition unless anticoagulants are used when there is an associated general pericarditis.

XII. CONCLUSIONS

1. The post myocardial infarction syndrome is a new recognizable major complication of recent myocardial infarction occurring at varying intervals after the acute infarction, with a striking tendency to recurrences.
2. The complication consists of one or a combination of the following; pericarditis, pleuropericardial pain, pleuritis, pneumonitis, and fever.
3. Hemorrhagic manifestations are another common characteristic of the syndrome.
4. The etiology is unknown but the complication may represent a hypersensitivity reaction to autoantigens that result from necrosis of the myocardium.
5. The exact incidence is not known but in the largest series it was believed to complicate 3% to 4% ofthe cases of acute myocardial infarction.
6. The main illnesses to be considered in the differential diagnosis are pericarditis epistenocardia, recurrent myocardial infarction and pulmonary infarction.
7. The clinical course is variable and the conditions most characteristic feature is its striking tendency

to recur; as many as 8 episodes have been observed.

8. The total duration is dependent on the number of recurrences and a case has been reported which persisted for 28 months.

9. Steroid therapy is the specific medication for the management of the condition but it is reserved for only severe, protracted cases, when pain cannot be controlled by other means or when there is rapidly spreading pneumonitis.

10. Most cases can be handled easily with symptomatic treatment.

11. Anticoagulant therapy, except for selected cases, is contraindicated when generalized pericarditis is present.

12. The prognosis is excellent in all but the cases where anticoagulant therapy is used in the presence of generalized pericarditis.

BIBLIOGRAPHY

1. Levine, S. A., Clinical Heart Disease, 5th Edition, Philadelphia, W. B. Saunders Co. 1958, p. 72.

2. Friedberg, C. K., Diseases of the Heart, 2nd Edition, Philadelphia, W. B. Saunders Co. 1956, P. 505, 517.

3. White, P. D., Heart Disease 4th Edition, New York, The Mac Millan Co. 1951, p. 534.

4. McGuire, Johnson and others, Acute Pericarditis, Circulation 9:425, 1954.

5. Dressler, William, A Complication of Myocardial Infarction Resembling Idiopathic, Recurrent Benign Pericarditis, Circulation 22:697, 1955.

6. _____, A Post Myocardial Infarction Syndrome: Preliminary Report of a Complication Resembling Idiopathic, Recurrent, Benign Pericarditis, J. A. M. A. 160:1379, 1956.

7. _____, The Post Myocardial Infarction Syndrome: A Report on Forty-four cases, A. M. A. Arch. Int. Med. 103:28, 1959.

8. Cohen, Goodman and others, Pleurisy and Pericarditis Complicating Myocardial Infarction : The So-Called Myocardial Infarction Syndrome, Canad. M. A. J. 82:123, 1960.

9. The PostmyocardialInfarction Syndrome, Am. Heart J. 59:632, 1960.

10. Weiser, N. J. and others, Postmyocardial Infarction Syndrome, Circulation 20:371, 1959.

11. Stein, Isidore and Weinstein, Joseph, Pericarditis Complicating Myocardial Infarction, 54:146, 1957.

12. Mandel, William and Johnson, E. C., Pleuropericardial Effusion Following Myocardial Infarction, Am. Heart J. 53:145, 1957.

13. Jones, L. O., The Post Myocardial Infarction of Dressler : Case Report, North Carolina Med. J. 21:142, 1960.

14. McGuire, Johnson and others, Nonspecific Pericarditis and Myocardial Infarction : Their Differential Diagnosis, Circulation 14:874, 1956.

15. Connolly, D. C. and Burchell, H. B., Pericarditis : A Ten Year Survey, Am. J. Cardial 7:7, 1961.

16. Jaffe, H. L., Pericarditis and Pleuritis in Acute Myocardial Infarction, J. Mt. Sinai Hosp. New York 27:40, 1960.

17. Likoff, William, Pericarditis Complicating Myocardial Infarction, Am. J. Cardiol. 7:69, 1961.

18. Dressler, William and others, Pericarditis Following Mild or Silent Coronary Episodes : An Attempt at Narrowing the Field of Idiopathic Pericarditis, Am. Heart J. 60:721, 1960.

19. Dressler, William, Coronary Pericarditis, Circulation 20:687, 1959.

20. Zinsser, H. F., Idiopathic Pericarditis, Mod. Concepts Cardiovas. Dis. 29:611, 1960.

21. Sodeman, W. A. and Smith, R. H., A Re-evaluation of the Diagnostic Criteria For Acute Pericarditis, Am. J. M. Sc., 235:672, 1958.

22. Epistein, Samuel, Is the Postcommissurotomy Syndrome of Rheumatic Origin?, A. M. A. Arch. Int. Med. 99:253, 1957.

23. Dressler, William, Idiopathic Recurrent Pericarditis. Comparison with the Postcommissurotomy Syndrome; Considerations of Etiology and Treatment, Am. J. Med. 18:591, 1955.

24. Ito, Tomiko and others, Postpericardiotomy Syndrome Following Surgery For Nonrheumatic Heart Disease, Circulation 17:549, 1958.

25. Evans, Elwyn, Introduction : Symposium on Pericarditis, Am. J. Cardiol. 7:1, 1961.

26. Engle, M. A. and Ito, Tomiko, The Postpericardiotomy Syndrome, Am. J. Cardiol. 7:73, 1961.

27. Dressler, William and others, Hemorrhagic Pericarditis, Pleurisy, and Pneumonia Complicating Recent Myocardial Infarction, Am. Heart J. 54:42, 1957.

28. Davies, A. M. and Gery, Igal, The Role of Autoantibodies in Heart Disease, Am. Heart J. 60:669, 1960.

29. Gajdusek, D. C. and Mackay, I. R., An "Auto Immune" Reaction Against Human Tissue Antigens in Certain Acute and Chronic Diseases, A. M. A. Arch. Int. Med. 101:9, 1958.

30. Lessof, M. H. and Asper, S. P., Autoantibodies, Am. Heart J. 59:473, 1960.

31. Gery, Igal and others, Heart Specific Auto-Antibodies, Lancet 1:471, 1960.

32. Harkary, Joseph, Vascular Allergy, Clinics 5:504, 1946.

33. Reference, Cited by Gery (33).

34. Dressler, William, Management of Pericarditis Secondary to Myocardial Infarction, Prog. Cardiovas. Dis. 3:134, 1960.

35. _____, Flare-Up of Pericarditis Complicating Myocardial Infarction After Two Years of Steroid Therapy, Am. Heart J. 57:501, 1959.

36. Reference, cited by Cohen (8).

37. Gillet, Robert, Acute Benign Pericarditis and the Coxsackie Viruses, New Eng. J. Med. 261: 838, 1959.

38. Carmichael, D. B. and others, Acute Nonspecific Pericarditis. Clinical, Laboratory, and Follow-Up Considerations, Circulation 3:321, 1951.

39. Goldstein, Robert and Wolff, Louis, Hemorrhagic Pericarditis in Acute Myocardial Infarction Treated with Bishydroxycoumarin, J. A. M. A. 146:616, 1951.

40. Tabatznik, Bernard and Isaacs, J. P., Post-pericardiotomy Syndrome Following Traumatic Hemopericardium, Am. J. Cardiol. 7:83, 1961.

41. Blumer, George, Pericarditis Epistenocardia, J. A. M. A. L07:178, 1936.

42. Stewart, C. F. and Turner, K. B., A Note on Pericardial Involvement in Coronary Thrombosis, Am. Heart J. 15:232, 1938.

43. Wolf, Louis, Diagnostic Implications of Pericardial, Pleural and Pulmonary Involvement in Cardiovascular Disease, New Eng. J. Med. 244:965, 1951.

44. Dressler, William, Pericarditis After Acute Myocardial Infarction, J. A. M. A. 173:1225, 1960.

45. Scott, R. C. and others, Nonspecific Pericarditis and Myocardial Infarction : Their Differential Diagnosis, Circulation 14:874, 1956.

46. Ellis, R. V. and McKinlay, C. A., Allergic Pneumonia, J. Lab. and Clin. Med. 26:1427, 1941.

47. McKinlay, C. A., Allergic Carditis, Pericarditis, and Pleurisy : Report of a Case of Serum Sickness with Predominant Cardiac Manifestations and Symptomatic Recovery, Journal-Lancet 68:61, 1948.

48. Geever, E. F. and others, Atypical Pulmonary Inflammatory Reactions, Dis. Chest 19:325, 1951.

49. Rich, A. R., and Gregory, J. E., On the Anaphylactic Nature of Rheumatic Pneumonitis, Bull. Johns Hopkins Hosp. 73:465, 1943.

50. Harkary, Joseph, Vascular Allergy, A. M. A. Arch. Int. Med. 67:709, 1941.

51. Anderson, M. W. and others, Hemopericardium Complicating Myocardial Infarction in the Absence of Cardiac Rupture, A. M. A. Arch. Int. Med. 90:634, 1952.

52. Barnes, A. R., Electrographic Pattern Observed Following Acute Coronary Occlusion Complicated by Pericarditis : Reports of Cases, Am. Heart J. 9:734, 1934.

53. Lagendorf, R., The Effect of Diffuse Pericarditis on the Electrocardiographic Pattern of Recent Myocardial Infarction, Am. Heart J. 22:86, 1941.

54. Hull, Egor, The Electrocardiogram in Pericarditis, Am. J. Cardiol. 7:21, 1961.

55. Steingberg, Israel, Roentgenography of Pericardial Disease, Am. J. Cardiol. 7:33, 1961.

56. Levy, R. L., Diseases of the Coronary Arteries and Cardiac Pain, New York, The MacMillan Co., 1936, p. 212, 215.