Acute Pericarditis

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The pericardium reacts to inflammation in a manner similar to that of other serous membranes by the production of a fibrinous exudate and varying types of effusion. The degree and character of the response vary with the noxious agent and condition the clinical manifestations which result. Pericarditis may represent the only cardiac lesion or it may develop concomitantly with myocarditis and endocarditis, although in most instances the superficial layer of the myocardium is involved to a variable degree. Pericarditis may be a primary disease or may represent one manifestation of a more widespread process. This review will deal with the clinical manifestations of the more important etiologic types of acute pericarditis.

Acute pericarditis may be classified etiologically into the following types:
1. Acute nonspecific pericarditis
2. Tuberculous pericarditis
3. Rheumatic pericarditis
4. Uremic pericarditis
5. Pericarditis secondary to myocardial infarction
6. Pyogenic pericarditis
7. Traumatic pericarditis
8. Pericarditis due to neoplasm
9. Other rare forms of pericarditis

Clinical Features and Pathologic Physiology

The various findings which fall under this heading and which are common to almost all types of pericarditis will be discussed before considering the individual etiologic types in more detail.

Subjective Symptoms

1. Pain. This symptom is extremely variable in its occurrence, distribution and intensity. The character of the pain varies in the different forms of pericarditis and will therefore be described later in greater detail under the specific etiologic type. The work of Capps,1 although somewhat at variance with the findings of Alexander and associates,26 has clarified the pathogenesis of pericardial pain. Capps found that the visceral and inner surface of the parietal pericardium are insensitive to pain. The outer surface of the parietal pericardium is insensitive above the fifth or sixth intercostal space. Pain fibers from the phrenic nerve are distributed over the outer surface of the parietal pericardium below this level since stimulation resulted in pain over the trapezoid ridge, characteristic of diaphragmatic pleurisy. In pericarditis the sharp pain, intensified by breathing, is otherwise not caused by the pericarditis per se but by contiguous involvement of the mediastinal, diaphragmatic or costal pleura. A large pericardial effusion may produce a dull oppressive sensation.

2. Symptoms which May Develop from Pericardial Tamponade. These include dyspnea, edema and ascites, right upper quadrant and

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epigastric pain due to hepatic congestion, fatigue, weakness and a sensation of faintness resulting from diminished cardiac output. Dyspnea is only rarely associated with pulmonary congestion but may develop from mechanical compression of trachea and bronchi, reduction in the vital capacity by encroachment of a huge pericardial effusion on the available intrathoracic space, or by associated pulmonary or pleural disease. Cough may occur as the result of one or more of the same mechanisms and hoarseness, dysphagia or hiccup may result from pressure on the esophagus or on the vagus or phrenic nerves.

3. General symptoms. Such symptoms as fever, malaise and anorexia may be the result of the pericardial inflammation or of the systemic disease with which the pericarditis is associated.

Physical Signs

A friction rub, heard by auscultation and occasionally felt by palpation, may be the only physical sign of fibrinous pericarditis. If pericardial fluid completely separates the parietal and visceral pericardium the rub disappears; however adhesions may prevent complete separation so that the sound is frequently audible in the presence of large effusions.

A pericardial friction must be differentiated from a pleuropericardial rub, from a xiphosternal crunch and from mediastinal emphysema. Harsh murmurs occasionally simulate a pericardial rub. A superficial to-and-fro friction sound may be heard at the base of the heart in acute cor pulmonale due to impingement of the bulging pulmonary artery and infundibulum on the pericardium and overlying sternum.

With the development of pericardial effusion the heart sounds may become distant and the apical impulse diminishes or disappears. Palpation of the apical impulse well inside the border of cardiac dullness is of considerable diagnostic importance in differentiation of effusion from cardiac dilatation. Compression of the base of the left lung by the pericardial effusion may produce dullness and bronchial breathing in an area below the angle of the left scapula (Ewart’s sign).

The development of signs of cardiac compression or tamponade depends both upon the size of the effusion and the rapidity with which it develops. If the fluid forms sufficiently slowly, the parietal pericardium may stretch to accommodate a liter or more before compression interferes significantly with cardiac dynamics; an effusion of only 150 to 250 cc. may produce tamponade if it develops rapidly. With the development of tamponade an increase in venous pressure occurs with distension of the neck and hand veins and engorgement of the liver. Inspiratory swelling of the neck veins may be noted since the increased flow of blood into the thorax with inspiration cannot be accommodated in the compressed right auricle.

The systolic blood pressure falls during tamponade and the clinical manifestations of shock may supervene. Characteristically there is a greater diminution in pulse volume during normal inspiration. This may be detected by palpation or may require the use of the sphygmomanometer. The blood pressure may fall through a range of a few millimeters of mercury normally with inspiration, but a fall greater than 8 to 10 mm. is abnormal and has been referred to as pulsus paradoxus.

Pulsus paradoxus, an unfortunate misnomer, is an accentuation of a normal mechanism which may be outlined as follows. The return of blood to the right side of the heart is increased during inspiration both as the result of increased negativity of intrathoracic pressure and increased positivity of intra-abdominal pressure. The result is increased right ventricular stroke volume during inspiration. The increased inspiratory capacity of the pulmonary vascular bed is almost completely compensated by this increased right ventricular output. Therefore, the volume of blood returning to the left side of the heart is only slightly diminished during inspiration and the left ventricular stroke volume is consequently only slightly diminished. During expiration the right ventricular stroke volume is definitely decreased and the left ventricular stroke volume slightly increased as a result of a reversal of the mechanisms just described.26

Recently Burwell and his associates27 have
made simultaneous measurements of pressures in the femoral artery, femoral vein, pulmonary artery, pulmonary vein, right auricle, and pericardium during the experimental production of acute cardiac tamponade in dogs. They demonstrated that all intravascular pressures approached the same level of approximately 20 mm. Hg at which point circulation ceased. They found that femoral venous pressures were higher than right auricular pressures but that this veno-auricular pressure gradient gradually decreased throughout the experiment until the two pressures became equal at maximal tamponade. Pulmonary venous pressure likewise progressively increased and presumably there would be a diminishing gradient between pulmonary venous and left auricular pressure (not measured), which would become zero when circulation ceased. Many years ago Katz and Gauchat suggested that, when cardiac tamponade was present, the variations in pressure in the distended pericardial sac and in the auricles are less during respiration than the variations in pressure in the extrapericardial intrathoracic veins. This leads to a relative diminution of inflow into both auricles during inspiration. Thus the right ventricular stroke volume is enhanced to a lesser degree by increased venous return during inspiration than it is normally. The left ventricular stroke volume is diminished to a greater extent than it is normally during inspiration both because of the greater diminution of the pulmonary venous-left auricular pressure gradient and also because the increased inspiratory capacity of the pulmonary vascular bed is less completely compensated by right ventricular output.

Recently British workers have given an alternate explanation for the mechanism of pulsus paradoxus. Normally the inspiratory drop in intrathoracic pressure is equally applied to the left ventricle and to the pulmonary veins. Therefore, left ventricular filling pressure remains approximately constant during respiration and no material change in stroke volume results. Normally the right ventricular filling pressure increases because the systemic veins are largely extra-thoracic. This increases the stroke volume of the right ventricle during inspiration, but does not normally influence the filling of the left ventricle. When the pericardium is distended, the increased inspiratory filling of the right ventricle increases the intrapericardial pressure, hindering filling of the left ventricle. Consequently decreased left ventricular stroke volume occurs in inspiration.

Roentgen Findings

Small effusions may produce no roentgenographic change or may merely straighten the cardiac waistline. The cardiac silhouette may not enlarge significantly until 300 cc. or more of fluid accumulates. With increasing effusion the normal chamber contours disappear. With large effusions the pericardial shadow may assume a pear-shaped appearance. The pulmonary vascular markings are not increased, a sign of considerable diagnostic value.

Fluoroscopically the cardiac pulsations are usually decreased or even completely absent, but this is not a constant finding. Pulsations of the aortic knob sometimes remain normal, since this structure lies outside the pericardial sac. Roentgenkymography or electrokymography may be utilized to demonstrate these objective changes in pulsations.

Although pericardial effusion sometimes causes the base of the cardiac silhouette to widen when the patient is changed from the upright to the recumbent or Trendelenburg position, this sign may not be particularly helpful in differential diagnosis since the flabby heart of cardiac dilatation may produce the same finding. Pericardial effusion is best differentiated from cardiac enlargement by (1) striking changes in the heart size in a relatively short period of time, particularly if the lung fields remain clear (fig. 1), and by (2) marked impairment or complete absence of pulsations in the presence of normal lung fields. The pulsations of an enlarged heart are seldom diminished unless cardiac failure develops; the lung fields will then almost invariably become congested. In doubtful cases angiocardiography may be utilized to demonstrate the presence or absence of a fluid-filled
pericardial shadow adjacent to the dye-filled right auricle.3

Electrocardiographic Findings

Pericarditis may be manifested electrocardiographically in two ways: (1) S-T and T-wave changes resulting from subepicardial myocarditis.4-8 (2) Diminution in voltage.

Figure 2 illustrates typical electrocardiographic changes in pericarditis. In the acute stage the characteristic finding is S-T elevation in several or all leads. In rare instances the elevation may be confined to one standard lead or to one precordial lead. Unlike myocardial infarction, pericarditis does not produce reciprocal S-T depression. The degree of elevation is variable; it has been stated9 that 0.5 mm. may be significant in standard leads if serial tracings are taken. At onset the S-T segments are frequently concave upward in contrast to the convex or cove plane S-T segments of myocardial infarction.6-10 The T waves are usually tall and peaked at this time7 but may be dome-shaped.7-11 The S-T segments may then become horizontal and, usually in a few days, more rarely in a few weeks, return to the baseline. The T waves become flattened or inverted and remain so for a variable period of time depending on the course of the pericardial inflammation. The inverted T waves are usually seen in all three standard leads, leads I and II or leads II and III and in the majority or all of the precordial leads. After inversion of the T waves, the S-T segment may be curved convexly upward, resembling the classic cove-plane T wave seen in myocardial infarction.9,12 However, it has been reported that, in contradistinction to myocardial infarction, T-wave negativity seldom appears until the S-T segment has returned to the baseline.10

The amplitude of the electrocardiographic complexes is frequently diminished by pericardial effusion. The presence of effusion in the pericardial sac influences neither the speed with which the electrocardiographic abnormalities become apparent nor the duration of time which they persist.10 Diminution in amplitude cannot be correlated well with the size of tuberculous pericardial effusions, the effect of pericardial aspiration on electrocardiographic potential being variable.13

Pericardial Paracentesis

The indications for pericardial aspiration are (1) the relief of cardiac tamponade and (2) the collection of fluid for diagnostic purposes.

The sites most commonly suggested for aspiration are the apical, the subxiphoid, the fourth intercostal space in the right or left parasternal line and the posterior thoracic ap-
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approach in the midscapular line. The sites of election preferred by 21 leading cardiologists have been tabulated. The apical approach was favored by nine, the subxiphoid by eight, the right parasternal and the left parasternal by two each. The posterior approach is used only if a large effusion produced signs of pulmonary compression posteriorly and fluid cannot be obtained easily from one of the other sites.

The apical approach should not be used if there is left pulmonary or pleural disease. If infected pericardial fluid is suspected, aspiration at the apical site may result in pulmonary or pleural contamination; the heart is not covered by lung at the subxiphoid site and with care the peritoneal cavity can be avoided.

Techniques for performing pericardial paracentesis have been described elsewhere.14

ACUTE NONSPECIFIC PERICARDITIS

Acute nonspecific pericarditis, which may be defined as a serofibrinous pericarditis of unknown etiology, is a clinical condition which has been recognized with increasing frequency during recent years. The term nonspecific is perhaps the most commonly used designation,15-22 but there are numerous synonyms such as idiopathic pericarditis,23-24 acute benign pericarditis,25-27 acute serofibrinous pericarditis of undetermined cause28 acute pericarditis,29-31 acute pericarditis of benign type,3 acute primary pericarditis,32 fugitive pericarditis33 and epidemic pericarditis.34 Titles have frequently called attention to the simulation of myocardial infarction3,7-8,11,35-38 or to the association of the process with preceding or accompanying respiratory infection.39-43

As pointed out by Christian23 and others,50 the syndrome was recognized as early as 1854,41 but in many modern textbooks it is mentioned only briefly or not at all. However, beginning with the paper of Barnes and Burchell5 in 1942, the numerous case reports cited above have appeared.

Clinical Features

Age. One hundred twenty-six cases have been selected from reports7-8,11,16,17,20,29,26,28,31,32 dealing with unselected civilian populations.

Fig. 2. Serial electrocardiographic changes in a case of acute nonspecific pericarditis.
The average age of this group is 35 years. Although this mean age is undoubtedly lower than that of any comparable group of cases of myocardial infarction, there is considerable overlap as indicated by the fact that 9 of the above 10 reports included patients in the sixth decade, and in three series \(7, 11, 20\) several patients were over 60. The disease has been reported in infancy.\(^{23}\)

**Sex.** Ninety-six of the 126 civilian cases were males, an incidence of 76 per cent. A predominance of males is found in all reported series and the apparent relative frequency of the disease in military and veteran’s installations\(^{6, 21, 22, 25, 29, 30, 37, 39, 42}\) further attests to the predominant sex incidence.

**Race.** It is impossible to determine the relative racial incidence of nonspecific pericarditis, since, in the papers reviewed, race is either not stated or the racial distribution of hospital admissions is not given. However, a sufficient number of cases have been reported in Negroes to indicate that this condition must be considered in the differential diagnosis of tuberculous pericarditis, known to be prevalent in this racial group.

**Previous Respiratory Infection.** Numerous reports\(^{7, 14, 18, 19, 20, 22, 28, 35, 41}\) have stressed the frequency of respiratory infection preceding the development of pericarditis. In four of the larger series\(^{6, 7, 20, 28}\) consisting of 109 patients, the incidence was 66 per cent. The average interval between infection and onset of pericarditis was 12 days, but this interval ranged up to one or two months. The preceding respiratory infection is most commonly described as a “cold” or “upper respiratory infection.” Preceding pulmonary infection has been less commonly noted. When pharyngitis is present preceding the pericarditis, there is no evidence in the literature that this is streptococcal in nature.

**Symptoms.** The most prominent symptom is usually chest pain. This may have a sudden onset with almost immediate maximal severity or it may be intermittent for several days before attaining maximal intensity. In 111 cases collected from the literature\(^{7, 11, 20, 28, 31}\) an acute onset was present in 60 per cent. The complete absence of pain is rare but has been noted in isolated instances. The pain is characteristically intensified by deep breathing, coughing, swallowing or rotation of the trunk. It may be localized in the precordial or substernal regions or may radiate widely over the thorax, to the interscapular region, to the neck, or to the epigastrium. It may extend into the shoulders or into the arms, occasionally radiating into the fingers.\(^{28}\) The left arm is much more frequently involved than the right. The pain may last from a few minutes to several weeks. Extremely intense pain usually does not last for more than a few hours and gradually becomes more moderate in a few days.

The reported incidence of dyspnea is variable in the various series, but, as Wolff has pointed out,\(^{11}\) it is usually the rapid, shallow breathing associated with pain that interferes with respiratory movements. Rarely sufficient pulmonary congestion occurs to produce dyspnea. Orthopnea is relatively uncommon,\(^{20}\) although pain may be less severe in the sitting position.\(^{15}\) Cough is also a variable symptom, but is prominent when there is an associated respiratory infection.

Malaise is noted in the great majority of patients. Anorexia, nausea and vomiting are relatively infrequent.

**Physical Findings.** Fever of some degree is almost invariably present. The highest daily temperatures frequently reach 102 F. and may range up to 105 F. In the minority of cases the temperature does not exceed 100 F. Fever on the first day of the illness is exceedingly common\(^{28}\) and it has been stated that it is usually maximal on the first day.\(^{15}\) The duration of fever is quite variable,\(^{28}\) paralleling the course of the disease.

The outstanding physical finding is a pericardial friction rub. Its reported incidence is 70 per cent or higher in the larger series, and it has been postulated that this sign will invariably be present if the patient is carefully observed during all phases of his illness.\(^{15}\) It is frequently present on the first day of the illness and may be noted within a few hours of the onset of chest pain.\(^{11, 15, 20, 28}\) Moreover, the friction rub is usually of greater intensity and is heard over a wider area than the rub which develops during the course of myo-
cardial infarction. The mean duration of the rub was nine days in each of two series with total durations ranging up to 30 to 60 days. The friction sound is usually less intermittent than that which develops in myocardial infarction. Instances of the patient being subjectively aware of the friction rub at the onset of the illness have been recorded.

The heart sounds may or may not be distant; the absence of suppression of heart sounds in the presence of enlargement of the cardiac silhouette has been cited as evidence that the latter is caused by cardiac dilatation rather than by fluid. Gallop rhythm is rare but has been recorded. Disturbances of cardiac rhythm are infrequent.

The development of shock is infrequent especially when contrasted with its incidence in myocardial infarction. Signs of cardiac compression are somewhat more frequent, but only rarely is pericardial paracentesis required to combat tamponade. Although cardiac dilatation is thought to occur, manifestations of congestive failure are not common. Pulmonary findings, if present, are more often caused by an associated inflammatory process than by congestion. Pleural fluid occurs rather frequently; it is present on the left side or bilaterally, isolated right-sided effusion being rare.

**Laboratory Findings**

A polymorphonuclear leukocytosis with a white blood count exceeding 10,000 per cubic millimeter is found in the majority of cases but is not invariably present. Like fever it is usually present earlier than in myocardial infarction and is likely to persist longer, the average duration being reported as three weeks. The average peak white blood cell count in one series of 27 cases was 20,400 with the highest count reaching 55,000. In other case reports, the white blood cell count did not reach such high levels.

The sedimentation rate is elevated in almost all cases and parallels the clinical course of the illness. Except for an earlier onset of accelerated sedimentation in nonspecific pericarditis than in myocardial infarction, the test has no diagnostic value.

Blood, urine, throat and nasal cultures have shown no consistent findings. Urinary albuminuria has been very rarely seen. Anti-streptolysin studies have failed to show any definite relationship to the hemolytic streptococcus. Cold agglutinins were not found in those instances where the test was performed.

Pericardial paracentesis has been performed infrequently in this disease. Pericardial fluid obtained from 15 patients was hemorrhagic in nine cases and variously described as straw-colored, cloudy yellow and clear amber in the remaining. Information concerning the amount of fluid withdrawn is unfortunately scanty, but it has been given as 10 to 100 cc. in three cases, 90 to 160 cc. in four cases, and 10 cc. in one case. Only a single report of multiple aspirations from the same patient was found; four taps yielded 80 to 100 cc. on separate occasions.

Pleural aspiration has been performed in 11 instances. In 10 cases the fluid was straw-colored. Four of these 10 cases also had pericardial aspirations which demonstrated nonhemorrhagic fluid. In the eleventh case both the pleural and pericardial fluids were hemorrhagic.

Pericardial fluid has been studied bacteriologically with smears, cultures and guinea pig inoculations in 13 instances. Bacteria have not been demonstrated. Pleural fluid studies have likewise yielded no etiological agent. Reports of virus studies have not been found.

Pericardial fluid cytology has been variously and infrequently described but a lymphocytic reaction is often present.

**Roentgenographic Findings**

The cardiac silhouette is enlarged in 50 to 80 per cent of cases. A rapid change in size is frequently seen; this is helpful in the differential diagnosis from myocardial infarction. In general, clear lung fields in the presence of an enlarged cardiac silhouette favors the diagnosis of pericardial effusion. However, this sign may be less useful in nonspecific pericarditis since inflammatory changes
may be present in the lungs. As already noted, pleural effusion is common.

The cause of the enlargement of the cardiac silhouette is not clear. Many believe that it is caused predominantly by cardiac dilatation rather than by effusion.20, 28, 44 The usual lack of suppression of cardiac sounds, absence of signs of cardiac compression, and persistence of normal voltage in the electrocardiogram are cited20 as evidence against massive effusion. Perhaps the best evidence pointing to the predominance of myocardial dilatation over pericardial effusion may be based upon the amounts of fluid removed by aspiration. As noted above this is usually in the range of 100 cc. Roesler has stated that pericardial effusion may not be demonstrable roentgenographically until approximately 300 cc. accumulates.45 However, it has been pointed out that the usual absence of gallop rhythm and of congestive failure represents evidence against any marked degree of cardiac dilatation.19

Mild pneumonitis, usually basilar in distribution, may be present.

Electrocardiographic Findings

As outlined in the introduction, the electrocardiogram almost invariably shows changes in nonspecific pericarditis and is an invaluable diagnostic aid. The elevated S-T segments usually return to the baseline in a few days, occasionally in less than 24 hours.10 The elevation was not observed after the twelfth day in a series of 50 patients.20 After approximately a week the T waves begin to invert and remain inverted from a few days to several months. The T-wave changes may fluctuate from day to day.6 The QRS complexes are ordinarily not affected, but in the presence of pericardial effusion, the amplitude may be decreased.6 Q waves are not produced since the myocardial involvement is limited to the superficial epicardium.

Prolongation of the P-R, QRS and Q-T intervals have not been reported. However, premature contractions, auricular or ventricular, shifting pacemaker, and paroxysmal supraventricular tachycardia and auricular flutter have been occasionally observed in this disease.7, 11, 22, 25, 28

Clinical Course and Prognosis

The duration of the illness is extremely variable. In Levy's series,28 the average duration was seven and one-half weeks with a range of two weeks to three months.

The prognosis seems to be uniformly good. We have found only a single reported fatality.21 This resulted from tamponade which developed while the patient was on full therapeutic doses of anticoagulants, given because of the erroneous diagnosis of myocardial infarction. Necropsy revealed evidence of acute pericarditis with old and recent hemorrhage into the tense, distended pericardial sac.

Recurrent attacks develop, and the term "acute relapsing pericarditis" has been suggested.15 Recurrences developed in 20 of a combined group of 127 patients.15, 18, 20, 28, 32 Second attacks were suspected in other individuals but the evidence was not conclusive. Four recurrences were noted in each of two patients,20 and one patient had two recurrences, five weeks and three months after the first episode.28 In two patients recurrences occurred 8 and 10 years respectively, after the initial attack.28 Of the four recurrences described by Levy,28 only one was preceded by an upper respiratory infection (maxillary sinusitis). A friction rub and electrocardiographic changes developed in all, bilateral pleural effusion was present in one, but pericardial effusion could not be demonstrated in any. Recurrences are generally of less severity and shorter duration than the initial illness.20 Burchell19 has emphasized the frequency of recurrent precordial pains which sometimes persist long after the convalescence is otherwise complete and Carmichael and co-workers20 noted such symptoms in 10 of their 50 patients.

A number of authors have described long term follow-up observations consisting of 14 cases originally reported in 1942 and 29 additional patients followed from one to five years,15 45 cases followed for more than two years20 and 17 cases observed for more than two years.28 A significant number of these have been examined 10 to 18 years after the initial attack. The development of the clinical picture of chronic constrictive pericarditis has not occurred, but in one case, reported in detail.24
roentgenographic studies four years after the initial episode demonstrated calcium surrounding the apex of the heart and it was the impression of the fluoroscopist that the apical region pulsed with diminished amplitude.

Rarely the electrocardiographic abnormalities persist.20, 46

**Differential Diagnosis**

The entities which most frequently simulate acute nonspecific pericarditis are acute myocardial infarction and other forms of pericarditis. Differentiation from infarction is completely outlined in several publications.7, 8, 11, 22 The most important points are: (1) A pleuritic type of chest pain occurs in pericarditis. (2) The friction rub, fever and elevation of the white blood cell count and sedimentation rate develop earlier, frequently on the first day, in pericarditis. (3) The electrocardiogram shows significant differences as already described. (4) The cardiac silhouette often undergoes more rapid changes in size in pericarditis. (5) An antecedent respiratory infection occurs in a significant number of cases of pericarditis.

Differentiation of nonspecific from tuberculous pericarditis is extremely important in view of the prompt and prolonged therapy indicated in the latter. Before the advent of modern treatment, the different clinical courses of the two diseases usually made the correct diagnosis apparent. Prompt administration of antibacterial agents, however, produces a rather rapid defervescence of the specific tuberculous process so that the clinical course of the two diseases may be practically identical. The relative absence of precordial pain in tuberculous pericarditis has been cited as an important diagnostic point.19 The presence of other manifestations of tuberculosis is, of course, important, but frequently the infection involves only the pericardium. Therefore, bacteriologic studies are essential in the differential diagnosis so that pericardial aspiration should be performed in most instances before embarking upon a prolonged period of treatment for tuberculous pericarditis. The value of the technic of pericardial biopsy47 requires further study.

Rheumatic pericarditis is usually easily differentiated from nonspecific pericarditis by the absent or minimal pericardial pain in the former, the presence of other manifestations of rheumatic fever or of pancarditis, the history of previous episodes of rheumatic fever, and the demonstration of a preceding streptococcal infection by means of antistreptolysin or antihyaluronidase tests.

Pyogenic pericarditis produces purulent pericardial fluid and is usually secondary to other etiologically proven pulmonary disease; differential diagnosis is difficult only when the disease is modified by inadequate antibiotic therapy, instituted without previous bacteriologic studies.

Uremic pericarditis is easily differentiated, and the other forms of pericarditis described in this review will usually cause confusion only if they are not considered because of their rarity.

Other causes of chest pain such as pulmonary infarction, acute pleurisy of various types, angina pectoris, spontaneous pneumothorax, mediastinal emphysema, diaphragmatic hernia, acute abdominal conditions and radicular pain resulting from spondylitis or other spinal lesions must sometimes be ruled out.

**Etiologic Considerations**

Carmichael and co-workers20 have summarized presently held hypotheses concerning the etiology of nonspecific pericarditis as viral, tuberculous, allergic and toxic. There is no evidence for the latter. The occurrence of acute nonspecific pericarditis following upper respiratory infections strongly suggests the possibility of a hypersensitivity reaction.39 The absence of demonstrable bacteria, the benign course and the recently reported response to certain antibiotic agents suggest a viral etiology but the leukocytosis and the lag between the preceding upper respiratory infection and the manifestations of the disease are points against such a cause. The recent case report of recurring pericarditis, ultimately proved by culture of biopsied pericardial tissue to be tuberculous, raises the possibility of a tuberculous etiology in occasional instances.47 However, the infrequency of the development of overt tuberculosis following nonspecific pericarditis
strongly suggests that it is not the pericardial counterpart of idiopathic pleurisy with effusion since the latter is rather frequently complicated by a tuberculous pulmonary lesion.

**Treatment**

Although acute nonspecific pericarditis is a benign disease with respect to mortality, a therapeutic agent which could shorten the prolonged period of morbidity would be highly desirable. In recent years certain encouraging reports have appeared, but all must be evaluated in the light of the marked variability of the clinical picture.

Sulfonamides and penicillin have not been beneficial. Three cases improved while receiving streptomycin, suggesting a therapeutic effect but streptomycin has been considered to be ineffective by others. The administration of aureomycin has been associated with rapid clinical improvement in five cases but was ineffective in three cases. When terramycin was given to one patient, rapid clinical improvement occurred. A recent report has indicated that none of the antibiotics are effective.

To our knowledge only one patient has had a trial with steroids. Adrenocorticotrophic hormone was begun on the sixteenth day of illness after adequate trials of penicillin, chloramphenicol, Aureomycin and salicylates had produced no response. Twenty-four hours after starting corticotropin (ACTH) the temperature promptly fell, precordial pain diminished and the friction rub disappeared. This report should encourage further trial with steroids, but places an even greater responsibility on the attending physician to rule out tuberculous pericarditis where such therapy might be potentially harmful.

**Tuberculous Pericarditis**

In 1952 Herrmann and co-workers found tuberculosis responsible for 8.4 per cent of all types of pericarditis and in 1953 Reeves noted an incidence of 7.3 per cent among acute forms of pericarditis. These figures compare rather closely with a 10 per cent incidence of tuberculous among all types of pericarditis reported in 1901.

The majority of the cases are seen in males, especially Negroes. In 16 cases seen on the Medical Service of the Cincinnati General Hospital since 1948 the age varied from 17 to 71 years. While older patients are said to be particularly susceptible, all but six of these cases developed before the age of 40 years.

Although tuberculous pericarditis is generally considered to be secondary to infection elsewhere in the body, it often appears as the dominant and sole manifestation of this disease. Such cases, often designated as "primary" pericardial tuberculosis, ultimately present signs of infection elsewhere in the body if survival permits. Pericardial infection develops either from direct extension from caseous mediastinal or hilar lymph nodes, pleuritis or myocardial tuberculoma or by hematogenous dissemination from pulmonary, skeletal or urogenital lesions. Generalized miliary tuberculosis may become manifest sometime after the appearance of isolated pericardial disease.

The infection begins with fibrinous deposits on both pericardial layers and these increase to considerable thickness and roughness. A clear, gelatinous, serosanguineous or frankly bloody effusion forms in small to massive amounts and may fill the sac or remain loculated by adhesions. Caseation follows and the pericardial space may be obliterated in whole or part by a thick, tough membrane in which calcium deposits form as healing progresses. Miliary pericardial foci may be found without thickening of the membrane in the generalized, rapidly-fatal form of tuberculosis. Constrictive pericarditis is sometimes the sequel to healing. Although the etiology of chronic constrictive pericarditis cannot be ascertained at operation or autopsy in half the cases, White concluded that tuberculosis is the most likely cause.

The clinical picture and natural course of patients with tuberculous pericarditis are quite varied. The onset may not differ from that of other types of acute pericarditis; occasionally it may be followed by or lead to the recognition of tuberculous infection elsewhere. Less frequently it may herald generalized miliary spread. The pericardial infection may be fatal or may subside and heal without treatment, only to be followed by recurrence of tuber-
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Tuberculosis in another serous membrane or other organ. Occasionally the onset is masked by pre-existing pulmonary or mediastinal symptoms. In older patients with coronary arteriosclerosis the pericardial infection may be obscured by the development of congestive heart failure.

The onset of tuberculous pericarditis is ordinarily slow and insidious and may be masked by fever, weakness, weight loss and cough. Attention may be directed to the heart only when a large or rapidly accumulating effusion causes shortness of breath and edema or when precordial pain appears. The pain is often mild, occasionally absent or atypical, and rarely severe. Some patients tolerate large effusions without symptoms of tamponade, since the accumulation may occur slowly. Fever of moderate degree is the rule, and, when combined with otherwise unexplained cardiac complaints, should raise the question of tuberculous pericarditis.

A pericardial friction rub is heard in the majority of cases and may persist for a few days to several weeks despite the presence of an effusion. Cardiac rhythm is usually regular but various arrhythmias, including auricular fibrillation, may occur. Although pleural effusions and ascites may result from circulatory failure, they are more often due to tuberculous infection of these serous membranes.

Moderate anemia is occasionally found and the white blood cell count may be low, normal, or, occasionally, mildly elevated. The electrocardiogram almost always presents evidences of pericarditis; the pattern of subacute or chronic pericarditis is most often found, even in the earliest tracings. The pericardial fluid may be clear or turbid but is usually grossly bloody. The white blood cell count of the pericardial fluid may reach 6,000 or 8,000 cells per cubic millimeter, the majority being lymphocytes. Tubercle bacilli can be demonstrated either by direct smear, culture, or guinea pig inoculation in most of the cases. Pericardial biopsy has established the diagnosis when other methods failed in several reported cases and in one of our own patients.

The mortality rate of untreated tuberculous pericarditis is high (83 per cent to 90 per cent)\(^1\),\(^2\),\(^3\) and is influenced unfavorably by increasing age, demonstration of acid-fast bacilli in the pericardial fluid, Negro race, and extrapericardial tuberculous disease. Those who recover often develop pericardial constriction. Consequently, considerable interest is attached to recent reports indicating the value of streptomycin in reducing the mortality rate in this disease. While the total number of cases reported is still small, and the selection of cases for treatment and variation in the regimen of therapy renders comparison difficult, it would appear that the mortality has been significantly reduced with streptomycin therapy. It is impossible as yet to assess the additive value of para-aminosalicylic acid (PAS) and isoniazid.

Treatment schedules for active tuberculosis with antibacterial drugs have changed greatly in the past few years. The Veterans Administration formerly recommended 1.0 Gm. streptomycin intramuscularly and 12 Gm. para-aminosalicylic acid orally for a minimum of 120 days. At present, ptthusiologists prefer to give 1.0 Gm. streptomycin daily until the toxemia subsides, and then reduce the dose to 1.0 Gm. twice weekly. The sodium salt of para-aminosalicylic acid (up to 12 Gm. daily) and/or isoniazid (150 to 350 mg. daily) is combined with this therapy. The length of time that treatment should be continued will depend upon many factors but should extend several months beyond the point where the lesion appears stabilized.

Death in the treated cases has been attributed to circulatory failure from pericardial constriction, or to miliary or meningeal spread following cessation of therapy.

RHEUMATIC PERICARDITIS

Pericarditis, associated with active rheumatic fever, is considered one of the commoner types of pericardial disease and frequently enters into the differential diagnosis of fibrinous pericarditis or pericarditis with effusion. In earlier reports its incidence was considered to be second only to that of pyogenic pericarditis, but, in recent surveys,\(^4\),\(^5\) wide variation in frequency is noted, probably due to geographic factors.

Although clinical signs of pericarditis have
been reported in 7 per cent to 48 per cent of cases with acute rheumatic carditis, pathological evidence is present in practically every instance. The lesions vary in their severity to such a degree that exudative reactions, adequate to produce clinical signs, do not always develop. Localized lesions are most frequent over the posterior wall of the left auricle. Generalized pericardial involvement is more often found in severe, protracted attacks of rheumatic fever, or in those with recurrent infections. Fibrin deposition is the essential lesion in the active phase of rheumatic fever; serous effusion, containing leukocytes, red cells, and shreds of fibrin, is variable. In protracted infections the pericardial membranes may be considerably thickened and shaggy. Adhesion of the two layers with bands of varying thickness or with complete obliteration of the sac follows healing. The pericardium may become adherent to contiguous structures (accretio cordis) by extension of the rheumatic infection into the mediastinum. Localized calcification may occasionally develop. Modern authors agree that the syndrome of chronic constrictive pericarditis does not follow healed rheumatic infection.

The age incidence of pericarditis follows that of acute rheumatic fever, the majority of cases developing before the age of 40 years. As a rule, the patients are acutely ill and present signs of rheumatic infection in other serous membranes, particularly in the synovia of several joints, and in the myocardium and endocardium. Myocardial involvement is always present with pericarditis and may lead to heart failure and arrhythmias. Clinical signs of endocardial involvement may not be evident early in the acute attack unless previous rheumatic activity was present. However, valvular deformity, rather than myocardial or pericardial scarring, is the only important residual which determines future cardiac disability. Consequently, rheumatic pericarditis is clinically significant only during the acute attack.

Pericardial symptoms or signs may be an outstanding feature of active rheumatic carditis in patients who develop effusion or they may be only an incidental finding in those without effusion. Subternal or precordial pain or oppression, often aggravated by respiration, is common but usually not severe. A pericardial rub is generally heard, even in the presence of small effusions, and tends to persist for several days or longer. Postmortem study has indicated that the amount of the effusion rarely exceeds 300 cc. When cardiac enlargement, elevation of venous pressure and other signs of circulatory failure appear, myocardial failure is the usual cause rather than tamponade. Pleural effusion often develops and may be bilateral. Cardiac murmurs commonly appear during the course of the illness or may antedate the pericarditis and persist in the majority as recovery of the acute phase follows.

Electrocardiographic abnormalities are common but the changes typical of pericarditis are found in less than half of the cases, probably because of masking by myocardial disease or ventricular hypertrophy following valvular involvement. Elevation of the S-T segments in several leads is the usual finding and occasionally precedes clinical signs of pericarditis. The changes are often fleeting and may be missed unless electrocardiograms are repeated every few days. Low or diphasic T waves appear as the S-T segments return to the isoelectric line; definite inversion of the T waves in many leads is uncommon in this type of pericarditis.

The treatment of rheumatic pericarditis follows that of acute rheumatic fever with carditis. Salicylates and adrenal steroids have been reported to diminish the amount of effusion and hasten the disappearance of the pericardial rub, but the variable course of the disease often invalidates such conclusions. Aspiration for tamponade is rarely necessary, although Sutton felt that paracentesis lessened the respiratory embarrassment and precordial discomfort.

**Uremic Pericarditis**

The pericardium, as well as the pleura and peritoneum, may be involved in uremia associated with chronic renal disease. This form of pericarditis is recognized clinically during the terminal phase of uremia in about 10 per cent of cases, although pathological examination may reveal involvement in a greater
number. Uremic pericarditis develops most often in the last weeks or months of life but remissions, healing, and recurrences have been described.63 The pericardium presents a fibrinous exudate with varying amounts of serous or hemorrhagic effusion. Organization and fibrous adhesions may be found in cases of longer duration. As a rule, no organisms can be cultured from the fluid, although pathogenic bacteria may be found occasionally as in other organs and tissues in uremia.

The etiology of uremic pericarditis is unknown. Most authors favor chemical irritation since the effusion is usually sterile. Hyperkalemia apparently plays no part in the pathogenesis of the pericardial lesion. Myocardial lesions have been described in uremia64 but have not been found regularly in cases with pericarditis.

The diagnosis is usually made first by the detection of a pericardial friction rub which may become extremely loud and leathery in character. The pericarditis is usually painless, although the stuporous condition of most patients may preclude recognition of this discomfort. Infrequently, a dull aching may be noted and rarely severe pain. Because effusion is absent or small, tamponade is uncommon.

The electrocardiogram in uremic pericarditis often fails to reveal the typical changes seen in other types of pericarditis.65 Alterations in the ventricular complex may occur during development of this complication but these may be nonspecific or obscured by pre-existing patterns of ventricular hypertrophy, myocardial damage or hyperkalemia.

Treatment of the pericarditis is usually unnecessary except in the unusual case presenting considerable pain or effusion with tamponade.

**Pericarditis Secondary to Myocardial Infarction**

Localized or extensive fibrinous pericarditis, infrequently associated with serous or bloody effusion, appears in those cases of myocardial infarction in which necrosis extends to the epicardial layer. Although the myocardial infarct may be localized to the anterior, lateral or posterior wall of the heart, the pericardial reaction can be more widespread and even generalized.65 In such cases a pericardial friction rub is most commonly heard, even though the infarction is posterior or basal. Massive serous effusion, producing tamponade and necessitating paracentesis, has been noted rarely.66, 67 As healing occurs, the visceral and parietal pericardium usually become adherent over the infarcted area.

The pericardial friction rub heard after myocardial infarction is characteristically fleeting but may persist for several days when the pericarditis is extensive. Occasionally, early electrocardiograms may show widespread S-T segment elevations after myocardial infarction, rather than the more typical reciprocal depression in leads from opposing surfaces. This finding and a persistent, loud rub should alert the examiner to search for other signs of generalized pericarditis in myocardial infarction.

**Pyogenic Pericarditis**

Invasion of the pericardial sac by pyogenic organisms produces an acute suppurative reaction and thick fibrinous exudate over the membranes analogous to empyema. While pyogenic pericarditis is uncommon due to modern chemotherapy, it remains important because of its high mortality when unrecognized.

The pneumococcus, staphylococcus and streptococcus are the commonest etiologic factors and reach the pericardium by direct extension from the lung, pleura or mediastinum, by the blood stream, or through penetrating wounds. Purulent pericarditis has also occurred in meningococcemia, in tularemia infections and through perforation of subphrenic or liver abscesses through the diaphragm. The clinical disorders leading to pyogenic pericarditis include pneumonia with or without empyema, osteomyelitis, acute endocarditis, stab wounds, puerperal sepsis, genitourinary infections, and septicemia originating in a wide variety of disease states. Most of our cases have followed extensive pneumococcal pneumonia with bacteremia in which early treatment was neglected.

Recognition of pericarditis under these con-
ditions is usually difficult unless a friction rub can be heard or increase in size of the cardiac silhouette observed. The patients are acutely ill from the primary disease. Suspicious findings are dyspnoea which cannot be otherwise explained, cyanosis, increase in venous pressure or evidences of tamponade. Pericarditis should always be considered whenever any acute infection does not account adequately for continued signs of sepsis, particularly when bacteremia has been present.

Electrocardiography has been very helpful in recognition of this complication since S-T segment and T-wave changes occur regularly and often before clinical signs of pericarditis are noted. Increases in size of the heart outline are also useful if earlier chest roentgenograms are available for comparison. Pericardial aspiration should always be performed if pericardial effusion is suspected. Stained smears will reveal large numbers of polymorphonuclear leukocytes, red cells and occasionally bacteria. Culture of the fluid often discloses the offending organisms.

The prognosis of any disease becomes graver when complicated by pyogenic pericarditis but recovery may occur with vigorous and appropriate chemotherapy if the pericarditis is still in an early fibrinous or serous stage. When thick pus has formed, recovery is unlikely unless prompt surgical drainage is instituted.

Treatment will depend upon the type of infection and duration of the disease. Very early cases may be managed with parenteral chemotherapy and by aspiration and instillation of the appropriate antibiotic. More advanced infections should have open drainage in addition to chemotherapy as soon as the diagnosis is made or when the medical regimen appears ineffectual.

**Traumatic Pericarditis**

Penetrating and lacerating wounds of the thorax involving the heart are the common causes of traumatic pericarditis, although rarely severe contusion to the chest may produce pericardial injury with hemorrhagic pericarditis. Clinically traumatic pericarditis is suspected when pericardial friction rub is heard or acute tamponade develops after injury to the chest. It is important in such cases to remember that, while the x-ray films of the chest may reveal a heart apparently normal in size, fluoroscopy shows absent pulsations of the heart. This is due to the very rapid development of bloody effusion without sufficient time for the pericardium to stretch. In penetrating wounds of the heart the modern treatment consists first of aspiration and, if tamponade recurs promptly, thoracotomy and suture of the cardiac wound.

**Pericarditis due to Neoplasm**

**Primary Pericardial Tumors**

Primary tumors involving the pericardium are extremely rare. The benign types include lipoma, fibroma, and angioma. Primary pericardial mesothelioma, also known as endothelioma, endothelial carcinoma or celotheilioma, is a malignant tumor which may metastasize or invade locally. Only 23 cases have been reported up until 1947. Various forms of sarcoma may originate in the pericardium or may arise in the heart and invade the pericardium. Although sarcoma represents the only important primary malignant neoplasm of the heart, only 112 cases have been reported through 1950.

**Metastatic Pericardial Tumors**

A recent report has emphasized the relative frequency of tumors involving the pericardium. In a group of 500 patients dying of various forms of malignant disease, necropsies demonstrated cardiac invasion in slightly more than 20 per cent and pericardial involvement in 6 per cent. Lymphoma (including leukemia) and carcinoma accounted for the majority of metastatic pericardial tumors. Lung and breast were the most frequent primary sites of carcinoma, but thyroid, pancreas, and a variety of other organ-systems were also implicated. Malignant melanoma frequently metastasized to the heart. Cardiac invasion by all forms of malignant tumors was usually accompanied by other widespread metastases at autopsy.

Physical, radiologic or electrocardiographic signs of pericarditis suggest metastasis in any patient who has malignancy or has had pre-
Previous surgical removal of a primary lesion. Occasionally, however, metastatic pericardial involvement may represent the only obvious manifestation of an underlying neoplasm. The pericardial fluid may be serofibrinous or hemorrhagic, and tends to recur rapidly despite repeated paracentesis. The diagnosis is best confirmed by microscopic examination of suitably stained smears or pathologic sections of the sediment of pericardial fluid. Pericardial biopsy may be helpful in more obscure cases, especially when tuberculosis, representing a condition amenable to specific therapy, is a serious consideration in the differential diagnosis. A careful search should be made for a primary lesion as well as for lymph nodes accessible to biopsy.

Roentgen therapy or various chemical agents may be temporarily helpful depending upon the nature of the malignant neoplasm.

**Other Rare Forms of Pericarditis**

*Pericarditis in Disseminated Lupus Erythematosus*

In the course of this disease the clinical diagnosis of acute pericarditis is rarely made, although at autopsy serofibrinous and adhesive pericarditis are commonly found.

*Pericarditis Associated with Infectious Mononucleosis*

A recent report, describing pericarditis as another manifestation of infectious mononucleosis, has stressed the importance of searching for the hematologic and serologic abnormalities characteristic of this disease in all cases of pericarditis in which the etiology is obscure. That infectious mononucleosis could only infrequently be the cause of acute nonspecific pericarditis is demonstrated by the polymorphonuclear leukocytosis usually found in the latter.

*Cholesterol Pericarditis*

An extremely rare type of pericarditis has been described by Alexander in which the fluid within the pericardium contained a high concentration of cholesterol and resembled gold paint.

*Chylopericardium*

Chylopericardium due to an obstruction or injury of the thoracic duct has been described. In this condition milky pericardial effusion has been observed. It is important to differentiate this disorder from purulent pericarditis.

*Echinococcus Infections*

Cardiac involvement by hydatid cysts is rare. However, Devé reported 83 per cent of 137 cases of cardiac echinococcus disease in which the primary infestation was localized to the heart. Rupture of a cyst from the heart and the pericardium may produce acute pericarditis or effusion with its usual clinical findings.

*Fungus Infections*

The pericardium may be involved by extension from actinomycosis of the lungs or mediastinum. When this occurs the pericardial exudate is seropurulent or hemorrhagic. The diagnosis may be established by cultural means or by demonstrating the organisms of actinomycosis in smears from the pericardial exudate. Treatment of actinomycosis with penicillin and sulfonamides and, more recently, with the broad spectrum antibiotics has been shown to be of value.

Three cases of coccidioidal pericarditis have been reported recently. The diagnosis may be suspected when there is an accompanying pneumonitis together with a positive coccidioidin skin test, but ultimately it depends upon the demonstration of positive coccidioidal complement fixation and precipitin tests or recovery of the organism. There is no known treatment but spontaneous recovery may occur.

**Summary**

Statistical studies of the frequency of the different etiologic types of acute pericarditis may be misleading because of an increasing recognition of nonspecific pericarditis. In our experience this form is the most common in private practice, while on the wards of a general
hospital, tuberculous pericarditis is the most frequent variety. Despite improvements in diagnostic technics there still remains a significant number of patients with acute pericarditis, the etiology of which cannot be categorized accurately. This latter group will be narrowed only after further clinical description and laboratory study.

The diagnosis of nonspecific pericarditis should be made carefully because of similarity of its onset to that of myocardial infarction and its benign course with tendency to relapse. Tuberculous pericarditis merits early recognition because of the improved prognosis following prompt treatment. Rheumatic pericarditis is often a problem in children and adolescents and indicates serious cardiac involvement; in adults the clinical course is generally more severe. Pericarditis occurring in uremia and myocardial infarction is usually an incidental finding in the course of a more important disease. Pyogenic pericarditis is now a rare occurrence except in certain infectious states.

The treatment of acute pericarditis has been considerably improved by the introduction of the antibiotic drugs. The judicious use of pericardial paracentesis may be life-saving in certain instances or it may yield diagnostic information from which effective therapy can be instituted.

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Acute Pericarditis

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