PATHOPHYSIOLOGICAL ASPECTS OF PERICARDIAL DISEASE

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CONTENTS

The pericardium is a smooth mantle surrounding the heart and containing a small amount of fluid resembling urine.

...Hippocrates (1)

λα σιογ κηρ

...Homer (2)

It is related that certain men are born with hairy hearts, and that no others are of greater energy, for example, Aristomenes, the Messenian, who killed 300 Lacaedaemonians. Captured and escaping twice, when he was captured a third time, the Lacaedaemonians cut out his heart while he still lived, and a hairy heart was found.

...Pliny (3)

The covering of the heart, let it be said, cannot have its function described by one term, for it serves to keep the Heart moist to protect it from external injuries;.....when too much water accumulates in it, injury of the Heart results and when such (i.e. fluid) is lacking, it adheres closely to the Heart, even on all sides to it; since it also is attached to the diaphragm it is inevitable that the motion of the Heart is combined and united with it.....this must be regarded as a great impediment and inconvenience.....just as the Heart labours when affected by disease within, so it does when oppressed from without by disease of its covering. So it happens that when that same covering of the Heart is filled with an effusion, and the walls are compressed with water on every side, so that they cannot dilate to receive the blood; then truly the pulse diminishes until at length it is suppressed by even more water, when syncope, and death itself follows. Just as the accumulation of too much water harms the heart, so too does trouble come when the heart and the pericardium become everywhere adherent.

...Lower (1669) (4)

The principal cause of dangerous symptoms appears to arise from the occurrence of gradual contraction in the layer of adhesive matter which has been deposited around the heart, compressing its muscular tissue and embarrassing its systolic and diastolic movement, but more particularly the latter. The ventricles having become diminished in capacity, make up for this loss by the rapidity of their contractions.

...Chevers (1842) (5)

Paracentesis of the pericardium is an operation which, in my opinion, approaches very closely what some surgeons would term a prostitution of the surgical art and others madness.....Perhaps a later generation will think otherwise about it.....

...Bilroth (1875) (6)

Probably no serious disease is so frequently overlooked by the practitioner. Post-mortem experience shows how often pericarditis is not recognized, or goes on to resolution and adhesion without attracting notice.

...Osler (1892) (7)

It is traditionally emphasized that pericardial disease is observed more frequently on the autopsy table than at the bedside (7,8). Prior to the era of cardiac catheterization, cardiac surgery, nuclear cardiology, echocardiography and widespread use of antibiotics, pericardial disease was found clinically in less than 1% of admissions to a large general hospital and in approximately 5% of consecutive post-mortems at another large hospital (9,10). Subsequently, increased awareness, better diagnostic tools and prolonged longevity in systemic illness have improved the frequency of recognition of pericardial involvement in disease states.

Pericardial disease has interested medical observers for centuries, as can be seen by the series of quotations above (1-7). Battlefields and the gallows provided the sources for morphological observations for centuries. In the seventeenth century, not only were descriptions of pericarditis (11), haemopericardium (12) and pericardiotomy (13) published, but the remarkably astute observations of Richard Lower in 1669 on cardiac tamponade, pulsus paradoxus and constrictive pericarditis were published (4). The advent of the nineteenth century saw the establishment of physical diagnosis and the distinction between various forms of pericarditis and pericardial effusion by Corvisant (14). Laennec, Corvisant's student, was "unable to say, from experience, how far and in what respect, the cylinder (stethoscope) will assist the diagnosis of the disease" (15), which led to criticism by Broussais, who ridiculed Laennec for listening too much "avec son cylindre". Later Chevers (5) distinguished between constricting and nonconstricting pericardial adhesions (vide supra) and in 1874, Kussmaul published his classical bedside observations in compressive pericardial disorders of distended neck veins and pulsus paradoxus (16).

While complete descriptions of all forms of pericardial disease are beyond the scope of this review, causes of the different types of peri-

cardial involvement are tabulated for reference. The present discussion will be confined to certain pericardial diseases with special attention paid to the pathophysiological aspects of these abnormalities.

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NORMAL PERICARDIAL FUNCTION

Man appears to tolerate pericardiectomy and pericardiotomy well. Nevertheless, the pericardium appears to perform several physiological roles, particularly during cardiovascular stress (17). Functions attributed to the pericardium from experimental studies include prevention of overdilation of the heart, protection of the heart from infection and from adhesions to surrounding tissues, maintenance of the heart in a fixed geometric position in the chest, regulation of the interrelationship between the stroke volumes of the two ventricles, and prevention of right ventricular regurgitation when ventricular diastolic pressures are increased (18). Many of these experimental studies addressing the role of the pericardium in acute volume and pressure cardiac overload states have produced conflicting results (19-25).

Recently, Shirato and colleagues performed acute volume loading followed by acute afterload reduction studies on dogs before and several days after pericardiectomy (26). The results of their studies are shown in Figure 1. In the studies performed with the pericardium intact, the left ventricular pressure-segment length curve shifted upwards during volume loading and then downwards during subsequent sodium nitroprusside infusion. After pericardiectomy, the control pressure-segment length curve was essentially the same as that with an intact pericardium, and volume loading followed by afterload reduction yielded points that consistently fell along the same exponential curve. They concluded that (1) under normal circumstances the pericardium exerts little restrictive influence on the left ventricle and (2) the pericardium contributes significantly to the increased left ventricular diastolic pressure in acute cardiac dilation and to the fall in pressure during acute afterload reduction. They suggested that pericardial restriction is a factor in the elevation of left ventricular diastolic pressure in acute cardiac dilatation produced by overtransfusion, acute valvular regurgitation, myocardial infarction and other forms of acute heart failure. They also pointed out that these alterations in intrapericardial pressure may not be the only factors producing these hemodynamic responses (27). Furthermore, these findings would obviously be inapplicable to patients with chronic cardiac dilatation, who have previously been shown to have essentially normal intrapericardial pressures (28,29).

In summary, the functions of the normal pericardium may be divided into mechanical membranous and ligamentous, and details of these roles are listed in Table 1.

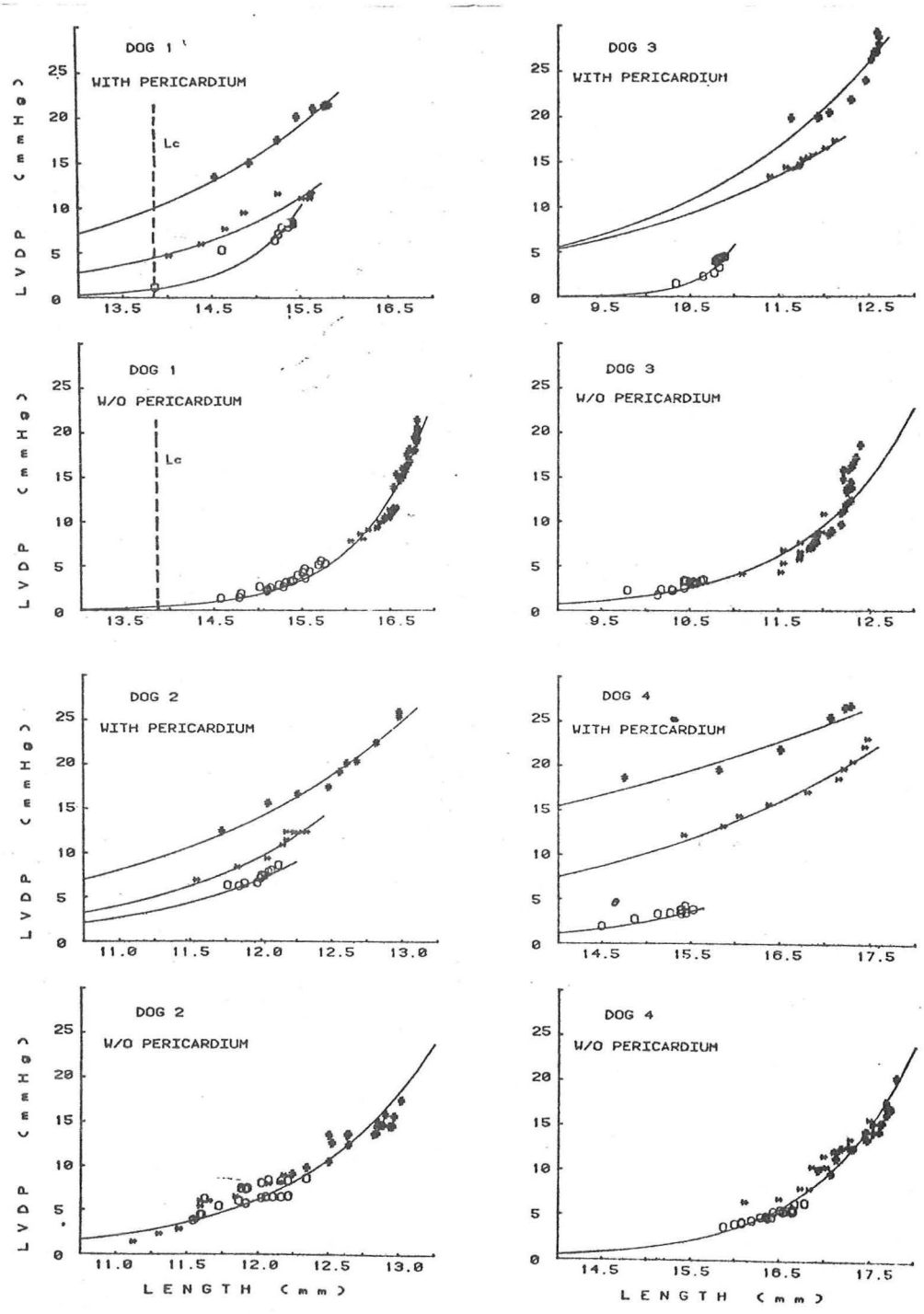

Figure 1: Left ventricular diastolic pressure-segment length curves before and after pericardiectomy in 4 dogs, where 0 = control values, # = after volume loading, and * = after sodium nitroprusside infusion (26).

TABLE I

FUNCTION OF THE PERICARDIUM

A. Mechanical function: promotion of cardiac efficiency, especially during stress.
   1. Limitation of excessive acute dilation
      (a) Defense of the integrity of the Starling curve
         (1) Maintenance of output response to venous inflow loads
         (2) Protection against excessive acute ventriculoatrial regurgitation
            Maintains ventricular function curves
            Limits effect of increased left ventricular end-diastolic pressure
            Favors equality of transmural end-diastolic pressure throughout ventricle, therefore uniform stretch of muscle fibers (preload)
         (3) Limits right ventricular stroke work during increased resistance to left ventricular outflow
         (4) Hydrostatic system (with pleural fluid) which constantly compensates for changes in gravitational and inertial forces.
      (b) Maintenance of output response to rate fluctuations
   2. Maintenance of functionally optimum heart geometry
   3. Provision of a closed chamber in which:
      (a) The level of transmural cardiac pressures will be low
      (b) Pressure changes aid atrial filling via negative pericardial pressure during ventricular systole
   4. Mutually restrictive chamber favoring equality of output from right and left ventricles over several beats
   5. Maintenance of normal left ventricular compliance (volume-elasticity relationship)
   6. Limits hypertrophy associated with chronic exercise.

B. Membrane function: shielding and heart
   1. Reduction of external friction due to heart movements
   2. Barrier to inflammation from contiguous structures
   3. Buttressing of thinner portions of the myocardium
      (a) atria
      (b) right ventricle
   4. "Feedback" circulatory regulation. Stimulation of:
      (a) neuroreceptors (via vagus)
      (b) mechanoreceptors

C. Ligamentous function: limitation of undue cardiac displacement

from Spodick (17)

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ETIOLOGY AND DIAGNOSIS

The various causes of acute and chronic pericardial diseases may be obtained from any standard test (31-33). Table 2 shows a useful morphological classification of some of the causes (33).

TABLE 2: Pericardial Disease: Morphological Classification

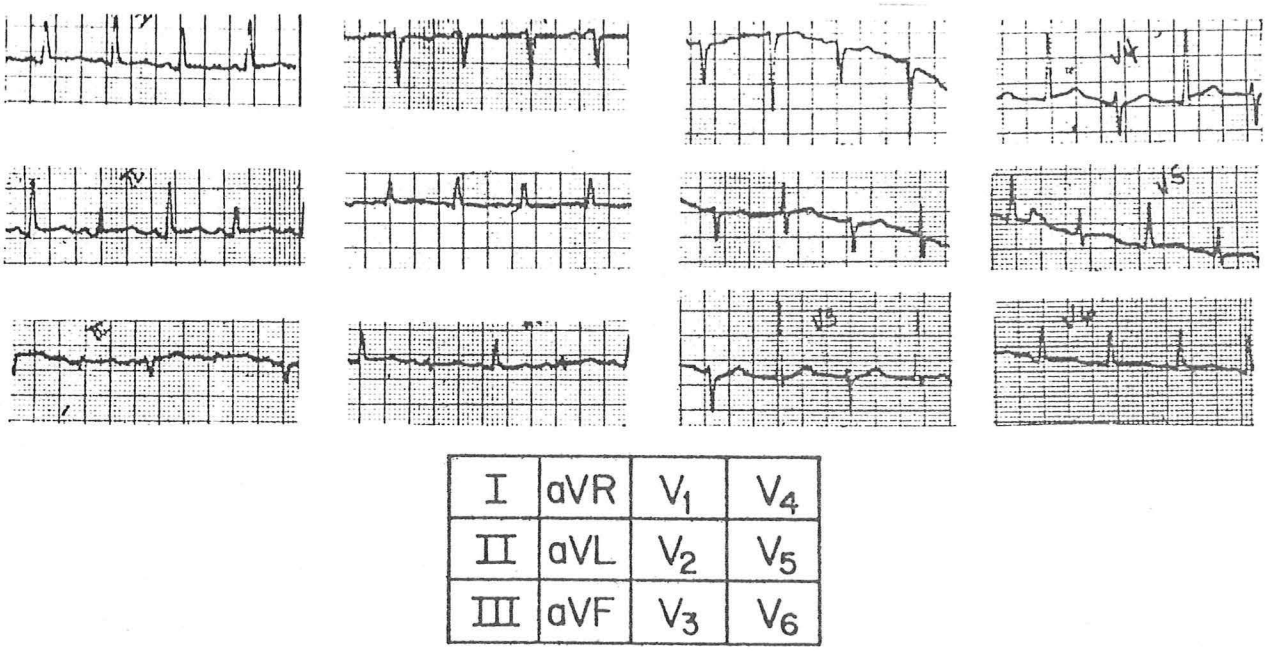
Etiologic	Morphologic: Fibrinous	Effusion	Infective	Fibrous	Neoplastic	Granulomatous	Calcific	Cholesterol
1. Idiopathic	++	+	0	++	0	0	++	++
2. Infective								
A. Pyogenic (purulent)	+	+	++	+	0	0	0	0
B. Tuberculous	+	+	+	++	0	++	+	+
C. Viral or "acute benign nonspecific"	++	0	+	+	0	0	0	0
D. Parasitic	+	+	++	+	0	+	+	0
E. Fungal	+	+	++	+	0	+	+	0
3. Associated with Systemic Disease								
A. Collagen disease								
1. Rheumatic fever	++	0	0	0	0	0	0	0
2. Rheumatoid arthritis	+	0	0	++	0	+	0	+
3. Systemic lupus erythematosus	+	+	0	++	0	0	0	0
4. Scleroderma	+	0	0	++	0	0	0	0
B. Renal disease	++	+	0	+	0	0	0	0
C. Thyroid disease	0	+	0	0	0	+	+	++
D. Sarcoidosis	0	0	0	0	0	++	0	0
4. Associated with Other Diseases of Heart or Aorta								
A. Acute myocardial infarction	++	0	0	+	0	0	0	0
B. Ascending aortic aneurysm	+	++	0	0	0	0	0	0
5. Trauma and Iatrogenic								
A. Penetrating and nonpenetrating injury	+	++	0	++	0	0	0	+
B. Cardiac catheterization	++	+	0	0	0	0	0	0
C. Cardiac operation and post-pericardiotomy syndrome	+	+	+	++	0	0	0	0
D. Resuscitation	+	+	0	++	0	0	0	0
E. Radiation	+	+	0	++	0	0	0	0
F. Drugs and hypersensitivity states	++	+	0	0	0	0	0	0
G. Talc	+	0	0	+	0	++	0	0
6. Neoplastic	+	+	0	0	++	0	0	0
7. Congenital								
A. True and false (diverticulae) cysts	–	–	–	–	–	–	–	–
B. Complete and partial absence	–	–	–	–	–	–	–	–

From Roberts and Spray (8)

The clinical manifestations of pericardial disease are both varied and well-known, and may be found in detail elsewhere (31,32).

The serial electrocardiographic changes in acute pericarditis of ST segment elevation in the limb leads in the absence of Q waves, with T waves that are firstly of increased amplitude followed by inversion, are both sensitive and specific (33). However, single electrocardiograms

are neither sensitive nor specific in patients with acute or chronic pericarditis. The electrocardiogram often shows only nonspecific changes or may be within normal limits. The typical increased ST vector (see Figure 2)



I	aVR	V_1	V_4
II	aVL	V_2	V_5
III	aVF	V_3	V_6

Figure 2: Electrocardiogram of a patient with cardiac tamponade, showing small but definite ST segment elevation in I, II, V_{4-6} and electrical alternans (31).

which parallels that major direction of the QRS axis in acute pericarditis is thought to be due to several mechanisms, although the principle hypothesis is that the changes are related to the underlying myocarditis (34, 35). The T wave changes of increased amplitude and subsequently inversion, the latter usually after the ST segment returns to the isoelectric line, are believed to reflect repolarization of the subepicardial myocardium which remains electrically negative while the rest of the myocardium is electrically positive (36).

Pericardial effusion may produce low voltage and cyclic variations in the amplitude of the electrocardiographic complexes (see Figure 2). This is thought to be due to the short-circuiting effect of the pericardial fluid (36). The original postulate that electrical alternans associated with pericardial effusion is apparently due to changes in cardiac position which results from pendular motion of the heart was confirmed by Feigenbaum's echocardiographic studies (37,38). The echo studies showed the anatomical position of the heart to shift with every other heartbeat, the so-called "swinging" heart (39) (Figure 3).

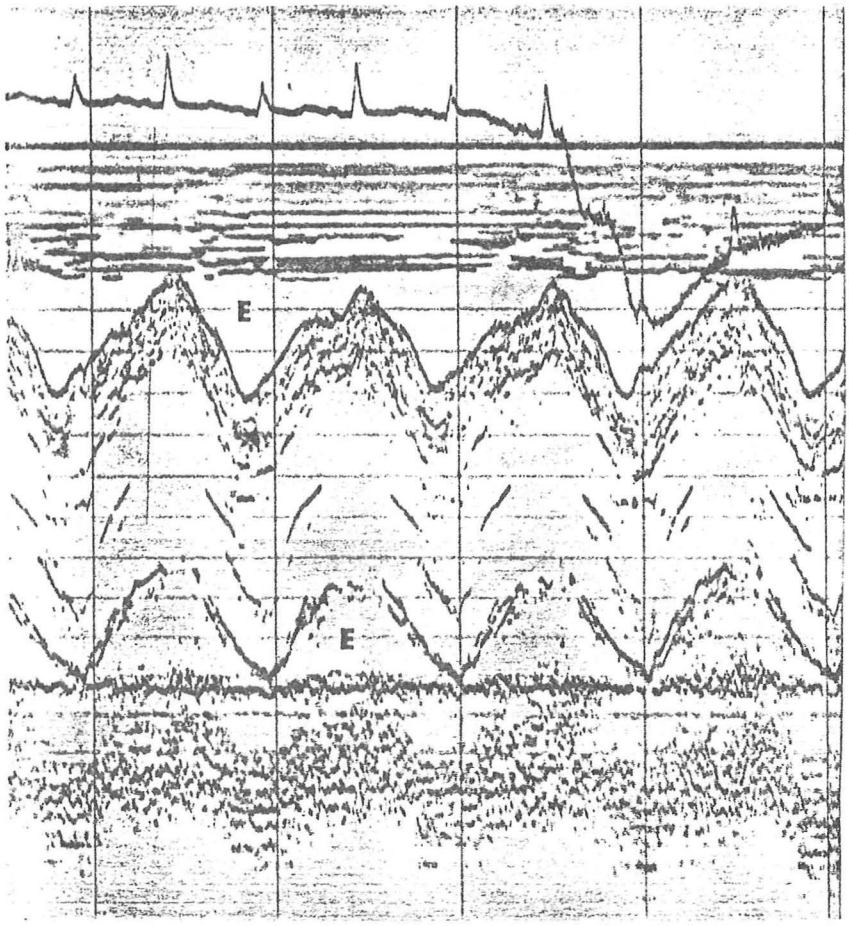


Figure 3: Echocardiogram of the "swinging" heart in a patient with a large anterior and posterior pericardial effusion (E), showing cardiac motion corresponding to two cardiac cycles and electrical alternans.

While large pericardial effusions may be diagnosed by a number of different techniques, including chest roentgenography, fluoroscopy, and radioisotopic blood pool scanning and angiocardiography, echocardiography is considered the optimal diagnostic technique (40-44). This is particularly so with small and moderate-sized effusions (45,46). While the existence of a pericardial effusion of greater than 15 ml is represented by a posterior echo-free space with or without an anterior echo-free space throughout the cardiac cycle, only gross estimates of the actual volume of fluid are possible by current techniques (45,47). Recently, the various echocardiographic characteristics of pericardial thickening have been reviewed and found to correlate significantly with morphological observations made at surgery or autopsy (48).

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CARDIAC TAMPONADE

The clinical features of cardiac tamponade are listed in Table 3.

TABLE 3: CLINICAL FEATURES OF CARDIAC TAMPONADE

Dyspnea
Orthopnea
Tachycardia
Elevated venous pressure
Decreased systolic blood pressure with narrow pulse pressure
Pulsus paradoxus
Heart Sounds: normal or feint
ECG: ST elevation or nonspecific T wave changes
electrical alternans
Chest X-ray: Cardiac silhouette normal or increased
lung fields clear.

from Fowler (44)

The conditions most commonly responsible for cardiac tamponade are trauma, neoplasm, infection and intrapericardial bleeding. Because the patient with tamponade may simulate one with congestive heart failure, the examination for pulsus paradoxus is most important. It should also be emphasized that in tamponade, the apical impulse is usually impalpable. A readily palpable and laterally displaced apical impulse associated with a prominent third heart sound are clinical features that favor congestive heart failure rather than cardiac tamponade (44). Sinus arrythmia tends to be reduced in tamponade (49). Furthermore, pulsus alternans may complicate severe tamponade. The status of the patient with cardiac tamponade may be modified considerably by either hypervolemia or hypovolemia and by the degree of sympathetic activity.

The hemodynamic alterations produced by cardiac tamponade are several (49) (Figures 4 and 5). Vena caval flow is reduced and systemic venus pressure is increased. A prominent x descent and corresponding peak of flow are seen in both venae cavae (Figure 4). The y descent is absent, and may be transformed into an abnormal positive wave of venous pressure.

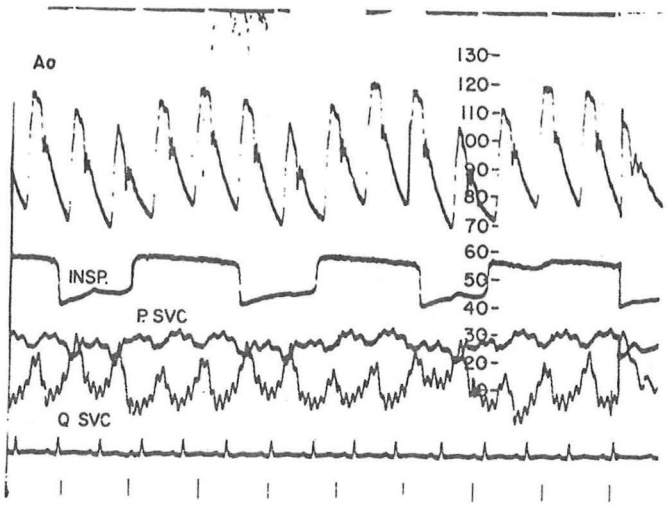

Figure 4: Superior vena caval (SVC) pressure (P) and flow (Q) and aortic (Ao) pressure tracings in a patient with cardiac tamponade. Note the pulsus paradoxus (aortic systolic pressure falls 15 mm Hg during inspiration). P-SVC (identical to the jugular venous pressure) shows a sharp x descent but no y descent (49).

This is explained by the fact that forward flow is confined to ventricular systole, and now occurs after the v wave of each cardiac cycle. Corresponding to the absence of the y descent, there is no early diastolic dip of the right ventricular diastolic pressure in cardiac tamponade (Figure 5). Inspiration is accompanied by a fall in vena caval pressure, and an increase in vena caval flow (50).

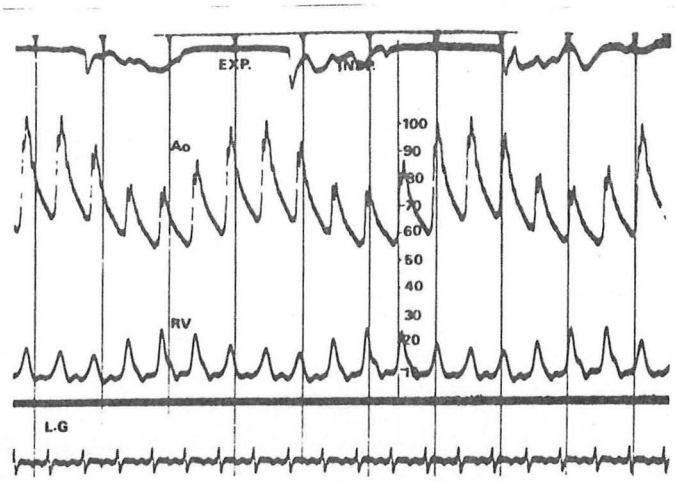

Figure 5: Right ventricular (RV) and aortic (Ao) pressure tracings in a patient with cardial tamponade. Note the pulsus paradoxus. RV pressure pulse has small amplitude and no early diastolic dip. RV systolic pressure is greater during inspiration and maximal RV pressure precedes maximal systolic Ao pressure by 3 cardiac cycles (49).

Recent studies of patients with cardiac tamponade using echocardiography have confirmed the experimental observations of inspiratory augmentation of right ventricular dimensions with concurrent reduction in left ventricular dimensions, and subsequent return to normal values after pericardiocentesis (56,57) (Figure 7).

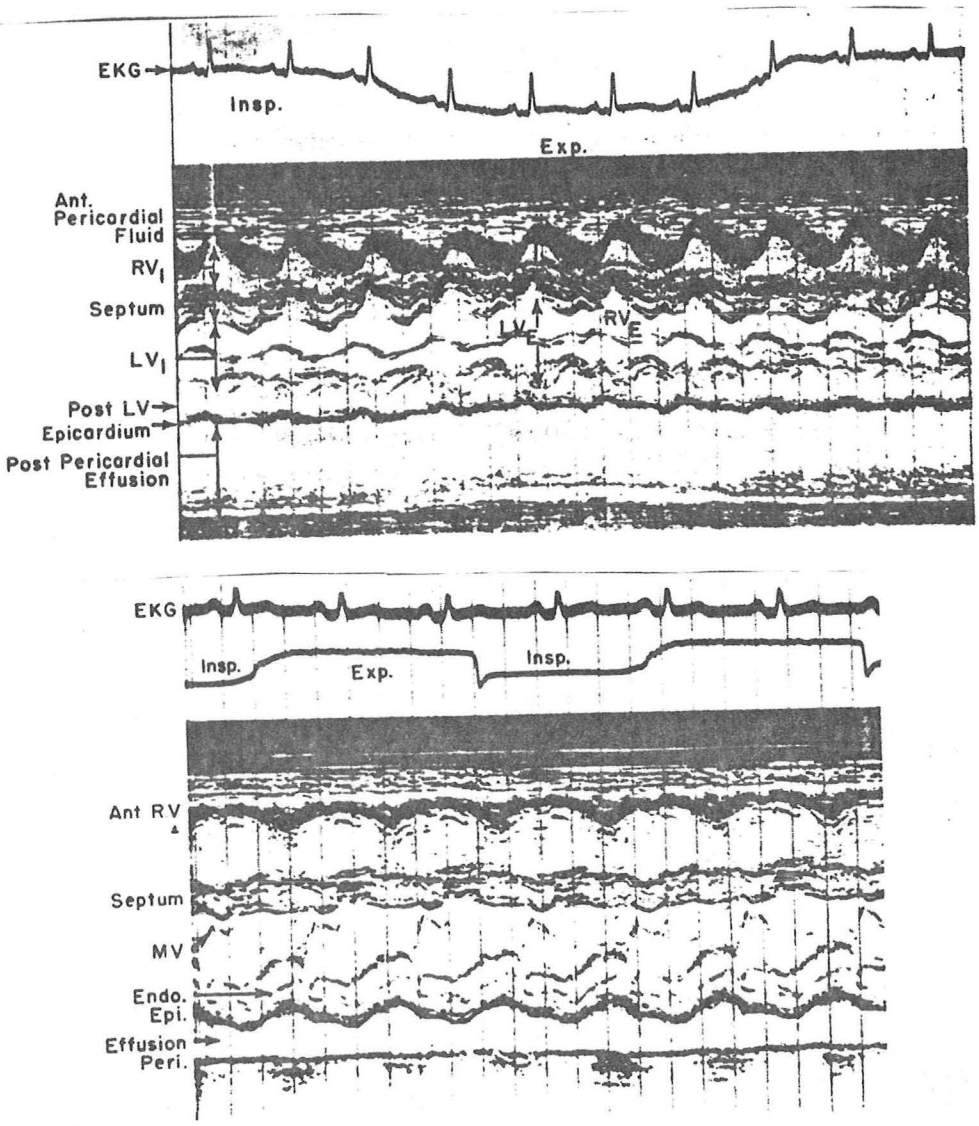

Figure 7: Echocardiograms of a patient with cardiac tamponade (upper) and after pericardiocentesis (lower). Note in the upper echo the effects of respiration on right ventricular (RV_1) and left ventricular (LV_1) diameters, which are absent after the removal of 500 ml of pericardial fluid (57).

In normal subjects, absolute pulmonary arterial pressure falls during inspiration (51). During mild or moderate tamponade, a similar inspiratory decrease occurs, whereas in severe compression an increase in pulmonary arterial pressure is seen (52).

Coinciding with the inspiratory increase in vena caval flow is augmentation of the right ventricular stroke volume with a decline in left ventricular stroke volume and systolic arterial pressure (53). The cycle of rising and falling left ventricular stroke volume was delayed by 2 to 3 cardiac cycles from the cycle of the right ventricular stroke volume.

The reduction in left ventricular stroke volume and thus cardiac output in cardiac tamponade produces a compensatory tachycardia. When the fall in stroke volume becomes greater than the compensating tachycardia, decreases occur in cardiac output and arterial pressure (54). It is only recently that the intrinsic cardiac mechanisms involved in tamponade have been elucidated. Pegram and her associates experimentally measured left ventricular internal end-diastolic and end-systolic diameters during increasing pericardial pressure using an ultrasonic dimension catheter (55)

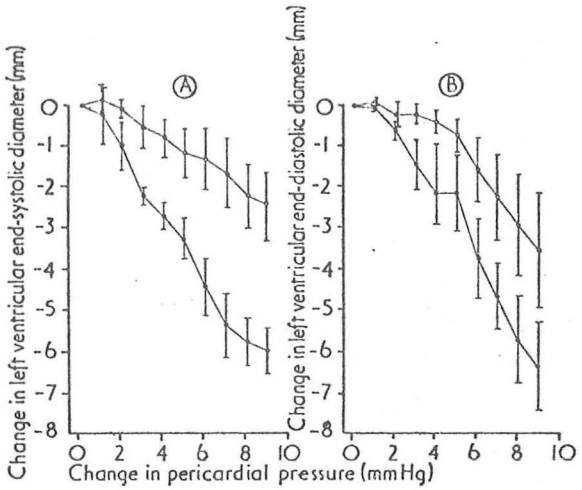

Figure 6: Changes in left ventricular end-diastolic (B) and end-systolic (A) diameters before (closed circles) and after (open circles) beta-adrenergic blockade with propranolol (55).

(Figure 6). They found a gradual reduction in both end-diastolic and end-systolic diameters, indicating both a Frank-Starling effect and an increase in contractile state. After beta-adrenergic blockade, at similar intrapericardial pressures, only a significant reduction in end-diastolic diameter was found. Their observations showed the importance of both the systolic reserve and the role of the beta-adrenergic receptors in the adaptation of the left ventricle to cardiac tamponade.

The effect of cardiac tamponade on coronary blood flow was demonstrated experimentally by O'Rourke and co-workers who showed a decrease in blood flow, and also a decrease in left ventricular myocardial work due to increased metabolic demands resulting from the induced tachycardia (58). They suggested the latter because the myocardial oxygen consumption was maintained during tamponade.

Effects of Pharmacological Interventions

The cardiac output of patients with tamponade may be increased by the intravenous infusion of normal saline or dextran (59). Isoproterenol has been shown to increase the cardiac output principly by its positive inotropic effect of increasing stroke volume rather than its positive chronotropic effect (59-61). Conversely, norepinephrine and acetylstrophanthidine have been ineffective (59,60). Because cardiac tamponade is associated with an increased peripheral vascular resistance, several afterload reducing agents have been examined experimentally and shown to be effective, including phenoxybenzamine, phentolamine, sodium nitroprusside and hydralazine (60,62,63). In a recently published study by Fowler and associates, hydralazine effectively increased cardiac output during tamponade, while nitroprusside only produced a similar increase after intravenous infusion (63).

While the importance of knowing the effects of these pharmacological interventions should not be underestimated, they are interim measures used prior to decompression of the tamponade by either pericardiocentesis or surgical resection.

Pulsus Paradoxus

Pulsus paradoxus may be defined as a greater than normal inspiratory decline in systolic arterial pressure. Because a slight inspiratory fall in arterial pressure is a normal phenomenon, an inspiratory decrease of 10 mm Hg or greater is considered abnormal (50,64). If the decline is greater than 15 mmHg, the inspiratory fall is often palpable at the peripheral pulses, and under extreme conditions, the arterial pulse may disappear completely during inspiration. Thus the term "paradox", as originally described by Kussmaul, is a misnomer (16). It is the degree of decline in arterial pressure, not the decline itself, that is abnormal. The causes of pulsus paradoxus are listed in Table 4.

TABLE 4: CAUSES OF PULSUS PARADOXUS

Cardiac tamponade
Constrictive pericarditis
Restrictive cardiomyopathy
Chronic obstructive pulmonary disease
Pulmonary embolism
Cardiogenic shock

from Fowler (44)

The hemodynamic mechanism of pulsus paradoxus in cardiac tamponade has been the topic of much investigation in the past few years. Earlier hypotheses included the suggestions that the normal inspiratory drop in intrapericardial pressure does not occur preventing the normal inspiratory increase in systemic venous return, that the respiratory descent of the diaphragm tenses an already taut pericardial sac decreasing left ventricular filling, and that augmented right ventricular filling displaces the interventricular septum thereby restricting left ventricular filling (65-68). Patient studies by Shabetai and colleagues confirmed some of the experimental findings and contradicted others (49). Their findings, which hemodynamically define pulsus paradoxus, may be summarized as follows:

(1) Systemic venous return is reduced in cardiac tamponade.
(2) Inspiration augments systemic venous return to a greater percentage than normal and thus produces a greater than normal variation in systemic flow (both venous and arterial).
(3) The increased inspiratory augmentation of right ventricular output is manifest in the systemic circulation two or three cardiac cycles later as an expiratory augmentation in systemic flow and pressure.

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PERICARDIAL CONSTRICTION

When involved by inflammation, fibrosis, calcification or neoplasm, the pericardium may become rigid and impede filling of the enclosed cardiac chambers. It is this condition that both Lower and Chevers were referring to in their classical seventeenth and nineteenth centuries descriptions. While chronic constrictive pericarditis has been known as

a distinct entity for many years, more recently a separate pathophysiological state of constriction combined with effusion has been described and entitled subacute effusive-constrictive pericarditis (67,69).

The clinical features of pericardial constriction are very similar to those of cardiac tamponade (vide supra). Differences include the occasional findings of a pericardial knock in diastole, atrial fibrillation and pericardial calcification on chest x-ray. It should be noted that these latter findings are typical of long-standing constrictive disease, and were not present in Hancock's series of younger patients with effusive-constrictive disease (69).

The hemodynamic alterations produced by pericardial constriction may be attributed to the decreased compliance of the so-called "lumped" system of the ventricles and the pericardium (49). The mean systemic venous pressure increases in proportion to the degree of constriction (Figure 8).

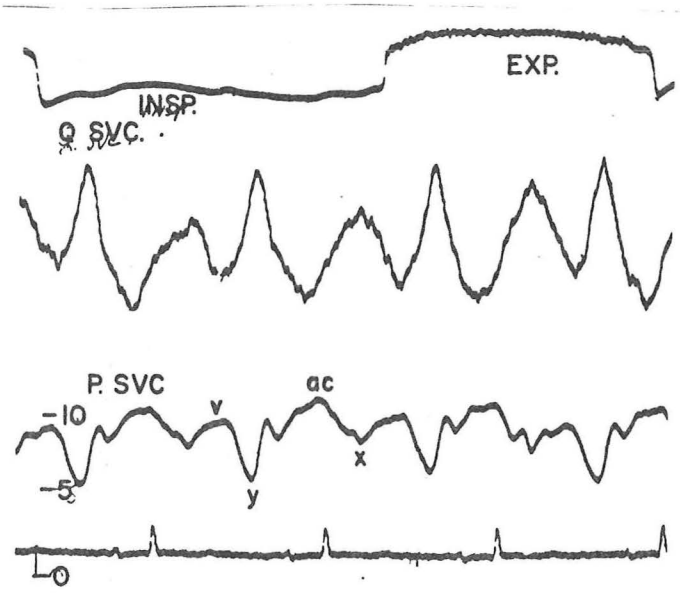

Figure 8: Superior vena caval (SVC) pressure (P) and flow (Q) in a patient with constrictive pericarditis. Note the deep x and y descents on the P tracing, the latter corresponding to the early diastolic dip of the right ventricular pressure, and the absence of respiratory variation in both P and Q (49).

A deep x descent corresponds to the beginning of ventricular ejection. The y descent is also deep and rapidly inscribed, and corresponds to the early diastolic dip of ventricular pressure. The venous pressure in late diastole is increased, equalling the elevated diastolic plateau

of the right ventricular pressure trace. The normal inspiratory increases in vena caval flow and decrease in vena caval pressure are diminished or absent (Figure 8). Occasionally, in patients with severe constriction, Kussmaul's sign is present.

Because ventricular filling as impaired, stroke volume is reduced. In early diastole, ventricular filling is rapid, but the limit of ventricular distensibility is reached prematurely. Thus, the right ventricular pulse tracing shows an early diastolic dip followed by a high diastolic plateau, the pressure of this plateau being more than one-third of the right ventricular systolic pressure (70)(Figure 9).

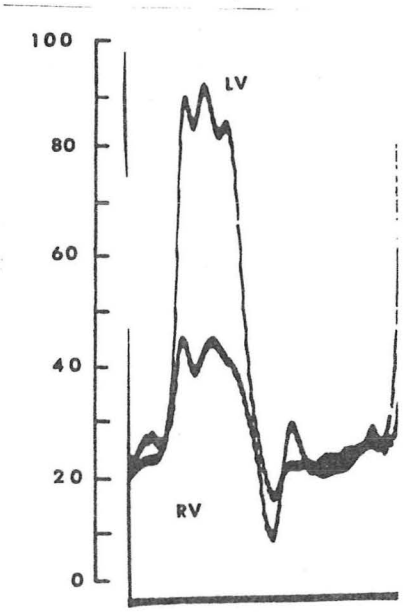

Figure 9: Left (LV) and right ventricular (RV) pressures in a patient with constrictive pericarditis. Note the early diastolic dip and late high plateau recorded from both ventricles (49).

Left ventricular volume studies on patients with constrictive pericarditis showed that, despite the reduction in end-diastolic volumes produced by the constrictive process, the contractile state as measured by ejection fraction and circumferential fiber shortening remained within normal limits (71).

Because of its value in serial follow-up, echocardiography has been utilized in assessing patients with constrictive pericardial disease. Feigenbaum has reported diastolic flattening of the posterior left ventricular wall, and a subsequent study reported abnormal interventricular septal motion (72,73). As mentioned previously, the echocardiographic features of pericardial thickening and constrictive pericarditis have

been reviewed recently, and concluded that while several findings were suggestive, none were diagnostic of pericardial constriction (49).

DIFFERENTIAL DIAGNOSIS

The differentiation between cardiac tamponade, pericardial constriction and restrictive cardiomyopathy may often be a diagnostic challenge. The hemodynamic and echocardiographic findings in these three conditions are summarized in Tables 5 and 6.

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MANAGEMENT

It should be reiterated that the optimal method of managing any form of pericardial disease causing cardiac hemodynamic compromise is a decompression procedure (45,64). Because cardiac tamponade constitutes a medical emergency, pericardiocentesis should be performed promptly and under the most ideal circumstances. While fluoroscopy is not essential, it is often useful (64). If the V lead of the standard electrocardiogram is utilized for guidance of the pericardiocentesis needle in the subxyphoid approach, the physician should be alerted to the dangers of accidental ventricular fibrillation from imperfectly grounded equipment (64,74).

In most patients with pericardial effusion, it is necessary to perform a pericardiocentesis on just one occasion. If recurrent cardiac tamponade has occurred or is considered likely, the necessity of repeated pericardiocentesis may be obviated by the insertion of a pericardial catheter (75-77). The conditions required for and the complications associated with the placement of a pericardial catheter would be identical to those of any intracavitary catheter.

TABLE 5: HEMODYNAMICS OF CARDIAC TAMPONADE, PERICARDIAL CONSTRICTION AND RESTRICTIVE CARDIOMYOPATHY

	Cardiac Tamponade	Pericardial Constriction	Restrictive Cardiomyopathy
1. Right Atrial (systemic venous) pressure	1. Usually elevated 2. *y* descent absent 3. Fall during inspiration	1. Elevated 2. Deep *y* descent 3. Little change during inspiration	1. Mildly elevated 2. Normal pressure display 3. Normal respiratory variation
2. Right ventricular pressure	1. Inspiratory augmentation 2. Elevated diastolic pressure 3. No early diastolic dip	1. No change in inspiration 2. Elevated diastolic pressure to >1/3rd systolic pressure 3. Consistent early diastolic dip	1. Normal respiratory variation 2. Elevated diastolic pressure, but <1/3rd systolic pressure 3. Early diastolic dip may disappear with therapy
3. Pulmonary capillary wedge pressure	Equals right atrial pressure	Equals right atrial pressure	Usually > right atrial pressure
4. Cardiac output	Reduced	Reduced	Reduced
5. Myocardial contractility	Normal	Normal or diminished	Diminished
6. Arterial pressure	Pulsus paradoxus	± Pulsus paradoxus	± Pulsus paradoxus

TABLE 6: ECHOCARDIOGRAPHIC FINDINGS IN CARDIAC TAMPONADE, PERICARDIAL CONSTRICTION AND RESTRICTIVE CARDIOMYOPATHY

	CARDIAC TAMPONADE	PERICARDIAL CONSTRICTION	RESTRICTIVE CARDIOMYOPATHY
1. Right ventricular diameter	Inspiratory augmentation	Normal	Normal or increased
2. Left ventricular end-diastolic diameter	1. Normal size 2. Inspiratory reduction	Normal	Normal or increased
3. Shortening fraction	Normal	Normal	Decreased
4. Mean Vcf	Normal	Normal	Decreased
5. Interventricular septal motion	Normal or Paradoxical	Paradoxical	Normal
6. Pericardium	Normal	Thickened	Normal or thickened
7. Pericardial effusion	Present	Present in effusive-constrictive disease; otherwise absent.	Absent

The continuing risk of recurrent cardiac tamponade or the diagnosis of constrictive pericarditis necessitates the partial or total removal of the pericardium (78-80). The choice between partial or complete pericardiectomy would clearly depend on the etiology of the pericardial disease and the likelihood of the development of pericardial adhesions or fibrosis.

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NEOPLASTIC PERICARDIAL INVOLVEMENT

Approximately 10% of patients with malignant neoplasms have some form of cardiac involvement, and 85% of these involve the pericardium (8). While the most common neoplasms with cardiac metastases in absolute numbers are carcinomata of the lung and breast, the tumors with the highest percentage of metastases are melanoma (70%), leukemia (37%) and lymphoma (24%) (81-83). Pericardial effusions, usually serous or serosanginous, may occur in lymphoma with equal frequency (about 15%) in the presence or absence of metastases (83).

Hodgkins Disease

While the literature is replete with anecdotes of pericardial involvement in Hodgkin's disease, the only reviews of this topic are of autopsy cases. Both reviews, one of 141 cases and the other of 196 patients, found the incidence of pericardial involvement to be 15% (83,84). Both series noted that occasional patients had morphological evidence of cardiac compression.

Radiation Pericarditis

The most common mediastinal tumor for which a patient is likely to receive sufficient therapeutic radiation to produce cardiac involvement is Hodgkin's disease (85). The incidence of pericardial involvement following radiation has been variously reported between 6 and 31% (86-88). It should be pointed out, however, that in these studies, the criteria for the diagnosis of pericardial involvement were morphological or surgical confirmation, or a significant increase in cardiac size on chest x-ray. Although earlier reports related the frequency of pericardial involvement to both the dosage and fractionation of the radiation, a subsequent larger study of 81 patients did not confirm these observations (85,86,89). This latter review reported the development of pericardial effusions in 25 (30%) of the 81 patients, and 22 patients did so within 12 months of completing upper mantle therapy (85). Approximately half of these patients had transient effusions and half had recurrent or persistent effusions. Half of the patients with persistent effusions or 7% of the 81 patients reviewed developed cardiac tamponade. The addition of chemotherapy did not affect the incidence or severity of the pericardial involvement.

The pericardial fluid, either serous or serosanginous, has a high protein content and low white cell count (85,86). The reports incorporating morphological data have described the presence of pericardial fibrosis in patients who developed either constrictive pericarditis or effusive-constrictive disease (86,90).

The recommended cardiac evaluation and follow up of patients with Hodgkin's disease after radiation therapy is outlined in Figure 10. Patients should be followed closely for 12 months after completion of radiotherapy,

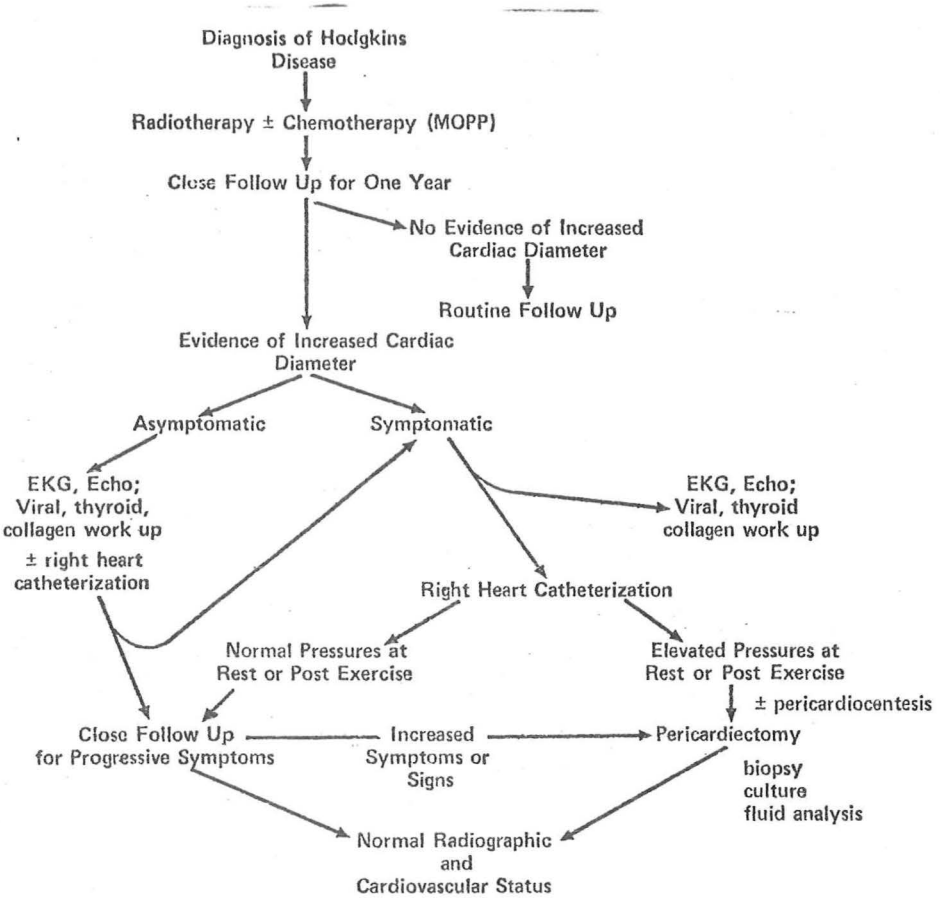

Figure 10: The current Baltimore Cancer Research Center recommendations for the diagnosis, evaluation and treatment of radiation-related pericardial effusions (85).

looking for the emergence of pericardial effusion. The physician should be alert to the possible development of cardiac tamponade. Patients with persistent or recurrent effusions should be considered for pericardiectomy because of the significant risk of subsequent cardiac tamponade (87).

The actual incidence of pericardial involvement of Hodgkin's disease and after radiation therapy is not known. The use of morphological data and radiographic criteria for the diagnosis of pericardial involvement obviously underestimates the incidence of involvement in both these circumstances. The only echocardiographic report published to date is of 10 patients with Hodgkin's disease, studied at Stanford, 6 of whom had pericardial effusions undetected by other means (91). After radiotherapy, pericardial involvement was detected on serial echo studies in 7 patients, only 2 of whom had no in-

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PERICARDIAL INVOLVEMENT IN CHRONIC RENAL FAILURE

The frequency of pericardial involvement in chronic renal failure depends upon the time of evaluation during the course of the patient's renal disease (92). In patients who present with chronic renal failure prior to dialysis, the incidence of pericardial involvement may be as high as 51% (93). Originally well known to be a preterminal event, pericardial disease in these

patients responds well to dialysis (92,94). The amount of effusion is small and the development of cardiac tamponade uncommon (94,95,96).

The incidence of pericardial involvement in patients on chronic hemodialysis is variously reported as from 10 to 16% in patients undergoing physical examinations and chest x-rays to 28% in patients who also had echocardiograms performed (92,96-100). The frequency of cardiac tamponade is much higher in patients on dialysis, and may be precipitated by the actual procedure (92,96). Baldwin and Edwards list the three primary causes of cardiac tamponade in these patients as (1) pericardial effusion (2) severe hemorrhage into the pericardial cavity, and (3) collagenization of the granulation tissue that organizes the fibrinous component of the pericardial exudate (94). Because the effusion may be either fibrinous or fibrous, the development of constrictive pericarditis is always a possibility and has been described both as an early and late complication (8,101, 102).

The management of patients with chronic renal failure should of necessity incorporate the use of echocardiography to alert the physician as to whether the pericardium is involved in the disease process. The development of cardiac tamponade requires prompt decompression with the insertion of a pericardial catheter if necessary. Recurrent or persistent effusions require further therapy. If the installation of nonabsorbable steroids (triamcinolone hexacetonide) does not reverse the continuing effusion, surgery should be performed (103). Partial or subtotal pericardiectomy is preferred to a pericardial window because of the nature of the pericardial involvement (104,105). The possibility of constrictive pericarditis developing in patients in whom surgery was not necessary to ameliorate their acute pericardial episode should be considered in the long term follow up of these individuals.

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PERICARDIAL INVOLVEMENT IN CONNECTIVE TISSUE DISEASE

Rheumatoid Arthritis

Although the incidence of pericardial involvement in rheumatoid arthritis at autopsy has been reported variously between 11 and 50%, a clinical diagnosis of involvement is relatively uncommon (106-108). In two prospective studies of patients hospitalized for rheumatoid arthritis, the respective incidence of pericardial involvement using clinical and radiological criteria were 10% and 2% (109,110). A retrospective study of all patients admitted to the Robert B and Peter Bent Brigham hospitals between 1949 and 1970 with rheumatoid arthritis revealed only 17 cases in whom typical cardiac enlargement on chest x-ray could be attributed to pericardial involvement by their primary disease (108). That these are underestimates of the true figures has been shown by two echocardiographic studies of patients with classical rheumatoid arthritis where 50% and 44% of the patients studied had well-documented pericardial effusions (111,112).

Pericardial effusions in rheumatoid arthritis, usually serous or serosanginous, contain a low sugar content, high titers of rheumatoid factor, high levels of lactic dehydrogenase and gamma globulin, and low complement levels (108,113)(Figure 11). They are associated with active disease (84%), positive rheumatoid factor (93%) and subcutaneous nodules (47%). Pericardial effusions are usually transient and uncommonly lead to cardiac embarrassment.

The frequency of hemodynamic compromise by pericardial involvement in rheumatoid arthritis has been reviewed recently (113). Only 20 cases of

cardiac tamponade and 46 cases of constrictive pericarditis have been reported. Both complications were more common in patients with active disease who had positive rheumatoid factors and subcutaneous nodules. Systemic steroid therapy neither failed to prevent nor led to the regression of either complication (113). Although pericardiocentesis is occasionally successful, it is frequently unrewarding because the pericardial fluid is often thick and loculated (114). Pericardiectomy, either partial or subtotal, is the treatment of choice for both cardiac tamponade and constrictive pericarditis in these patients.

Thus, while pericardial effusions are no doubt more common in patients with rheumatoid arthritis than was at first realized, they are essentially benign. The physician should be alert for the very occasional case of cardiac compression in patients with active rheumatoid arthritis.

Determinations	RA	SLE	SS
Number of cases	8	4	1
Source	19-21	22-24	Gladman (present report)
Appearance	Serous	Yellow-bloody	Blood-tinged
White cell count (mm^3)	950-88,100	1,280-30,800	400
Glucose (mg/100 ml)	14-65	61-90	108
Total protein (g/100 ml)	4.5-9.7	3.4-7.6	5.8
Immunoelectrophoresis	Increased gamma globulin	NA*	Normal
Latex test	Positive	Negative	Negative
Antinuclear factor	Negative	Positive	Negative
Lupus erythematosus	Negative	Positive	Negative
C_3	Normal or low	Low	Normal
CH_{50}	Low	Low	Normal
Cryoglobulins	NA*	NA*	Negative
Free DNA and DNA antibodies	NA*	NA*	Negative
Soluble immune complexes	Positive	NA*	Negative

*NA = not ascertained.

Figure 11: Comparison of the properties of pericardial fluid in rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE) and scleroderma (systemic sclerosis; SS) (120).

Scleroderma

Pericardial involvement in scleroderma is a common finding at autopsy, its frequency varying from 33 to 71% (115-117). Generally thought to be of little importance, a retrospective review of 210 patients found its clinical prevalence to be 7% (118). In the latter review, patients with pericardial

involvement were found to divide naturally into those with acute pericarditis and those with pericardial effusion. In patients with pericardial effusion, identified clinically, radiographically or echocardiographically, Raynaud's phenomenon was more common than expected and the demonstration of the effusion preceded the onset of renal failure in 6 of the 11 patients. Three of the 11 patients developed early clinical evidence of cardiac tamponade which did not require pericardiocentesis. In our study of 11 patients with scleroderma, 3 had small or moderate sized pericardial effusions by echo, and none of the 3 had evidence of chronic renal failure (119). All of our patients had Raynaud's phenomenon.

The pericardial fluid is either serous or serosanguinous, has a normal protein, glucose and complement level and a low white cell count (120) (Figure 11).

Whether hemodynamic compromise from cardiac tamponade or constrictive pericarditis occurs in these patients remains unclear. Only one morphological observation of constrictive pericarditis has been made (117). Thus, pericardial involvement in scleroderma seems relatively uncommon, and subsequent cardiac compression is probably rare.

Systemic Lupus Erythematosus

The prevalence of pericardial involvement in autopsy series of patients with SLE varies from 47 to 57% (121,122). The advent of corticosteroid therapy has resulted in the morphological observations of increased pericardial adipose tissue deposition and the alteration of the original typical fibrinous pericardial involvement to a fibrous type (122). Although relatively rare as an initial manifestation of the disease (1 to 4%), pericardial involvement during the clinical cause of SLE has been reported in 17 to 45% of patients (121). The clinical data were obtained using electrocardiographic and radiographic criteria. It is felt that pericardial involvement in SLE is an indicator of concurrent cardiac disease, especially Libman-Sacks endocarditis, although proof of the association, at present is confined to morphological studies (122,123).

Unlike rheumatoid arthritis, pericardial involvement in SLE does not appear to be related to the severity or activity of the disease (124). Pericardial effusions are serous or serosanginous with a high protein, normal or low glucose, low complements levels and positive LE preparation and antinuclear antibody (120,125)(Figure 11).

The incidence of cardiac tamponade in SLE is uncommon, quoted at about 7% of those with pericardial involvement (121). It may rarely be the initial manifestation of the primary disease (123). Cardiac tamponade has also been reported to occur in drug-induced lupus syndrome, due to procainamide, hydralazine and isoniazid (126-128). Constrictive pericarditis is quite rare (129).

Thus, although pericardial involvement is relatively frequent in SLE, cardiac tamponade is uncommon. Nevertheless, the physician should be alert for this complication in both spontaneous SLE and the drug-induced lupus syndrome.

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CONCLUSION

Homer's well-known phrase, "the hairy hearts of hoary heroes", indicates that not only has pericardial disease been a pathological entity of interest to physicians for thousands of years, but that early observers held romantic notions about its existence. The complications and their management have also been known for a similar period of time, confirmed by the reference in the Dead Sea Scrolls (before 1 A.D.) to the priest who died from his "hairy" heart because he had not undergone pericardiectomy. The clinical observations over the centuries coupled with the sophisticated techniques that are now available, permit the modern physician to make an early and accurate diagnosis.

Nevertheless, Sir William Osler's advice for the clinician remains appropriate to this day. The pericardium may be involved in disease in both primary and secondary forms. The disease process may cause hemodynamic compromise that, untreated, can be fatal. Both cardiac tamponade and constrictive pericarditis have distinguishing features that enable an accurate diagnosis to be made, and prompt treatment to be instituted.