Echocardiographic Evaluation of Pericardial Effusion in Myxedema
Incidence and Biochemical and Clinical Correlations

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SUMMARY
Pericardial effusion is a recognized consequence of myxedema. Its incidence is unknown, primarily because of past difficulties in establishing the diagnosis. We studied 33 hypothyroid patients by echocardiography. Ten of the 33 patients (30%) had positive echoes for pericardial effusion. Seven of these ten patients had enlarged hearts on chest X-ray. Five patients had cardiac enlargement but no echo evidence of pericardial effusion. Serum concentrations of thyroxine, 1.8 ± 0.3 vs 1.5 ± 0.1 mcg/dl and of thyroid stimulating hormone, 34 ± 4 vs 38 ± 5 mcg/ml did not differ in the groups with and without pericardial effusion, respectively. However, the pericardial effusion group had significantly slower heart rates on ECG than those without pericardial effusion: 53 ± 8 vs 68 ± 2 beats/min, P < 0.05. Low voltage was present in five of the ten patients with pericardial effusion and five of the 23 nonpericardial effusion patients. None of the patients with pericardial effusion developed tamponade. Seven patients with pericardial effusion were restudied after periods of thyroxine replacement therapy ranging from six months to two years. All were euthyroid and had negative echoes on follow-up, but two still showed cardiomegaly on chest X-ray (both had associated coronary artery disease). We conclude that pericardial effusion occurs frequently in patients with myxedema. Tamponade is uncommon and the effusions disappear with thyroid replacement therapy. Cardiomegaly on chest X-ray and low voltage on ECG are not reliable indicators of pericardial effusion.

PERICARDIAL effusion has long been known to occur in myxedema. However, little information is available about its incidence, relationship to clinical severity of hypothyroidism or to tests of thyroid function. This has been due to difficulty in the diagnosis of pericardial effusion which in the past involved procedures such as carbon dioxide or angioisotopic angiocardiography. Echocardiography has been used to detect pericardial effusions since 1965. This safe and accurate noninvasive technique has become the method of choice for the diagnosis of pericardial effusion, but has not previously been used to study patients with myxedema in a systematic fashion. We utilized echocardiography to obtain information about the incidence of pericardial effusion in myxedema, to establish correlations with other clinical and biochemical parameters of hypothyroidism and to ascertain the response to thyroid replacement therapy.

Methods
The subjects of this study were 36 patients seen at the University of Iowa Hospitals between March 1972 and July 1974 who had clinical and laboratory features of hypothyroidism. Although we attempted to study all patients at this institution who had the new diagnosis of myxedema, there may have been additional hypothyroid patients who escaped our notice. No attempt was made to select patients by age, sex, cardiac symptoms, severity of disease or other similar criteria, but it is possible that those referred for echocardiographic study exhibited more advanced signs and symptoms of thyroid hormone deficiency. The following studies were obtained on each patient: echocardiography, chest X-ray, serum thyroxine and serum thyroid stimulating hormone (TSH). Echocardiograms were performed using a commercially available ultrasonoscope (Smith-Kline Ekoline 20) and recorded either on Polaroid film or, in the latter part of the study, on a fiberoptic strip-chart recorder (Honeywell 1856). The ultrasonic transducer was directed to reflect off the posterobasal portion of the left ventricle, inferolateral to the mitral valve leaflets. The gain and sensitivity settings were manipulated to best define the relative position and motion of the pericardium, epicardium and endocardium and mitral valve and chordae.

Figures 1–3 show echocardiograms obtained in this study and illustrate our echocardiographic criteria for the diagnosis of pericardial effusion. These criteria were similar to those of Horowitz et al. when a single moving pericardial echo was visualized at low ultrasonoscope sensitivity, and no separation between epicardium and pericardium was seen as the gain was increased, the recording was considered to be negative for pericardial effusion (fig. 1). Definitely

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positive recordings were those in which the pericardial echo was flat and was separated from the moving epicardial echo by an echo-free space which persisted through the cardiac cycle (fig. 2). If the posterior echo-free space was large and an anterior echo-free space was also present (fig. 2), the effusion was considered to be large (in our experience and that of Horowitz et al., such patterns are associated with effusions in excess of 200 cc). An echo-free anterior space alone, without a corresponding posterior epicardial-pericardial separation, was considered to be negative.

Seven patients had intermediate recordings of the type illustrated in figure 3: a small systolic and early diastolic epicardial-pericardial separation was present, but the echoes merged in mid-diastole and the pericardial echo was not flat. This pattern is generally associated with very small (less than 16 cc) amounts of pericardial fluid, although in one of Horowitz’s cases 90 cc of fluid was present. For purposes of this study recordings such as these were considered negative, with the understanding that by applying such stringent criteria we may have failed to diagnose some small effusions.

In three patients the echocardiograms were not of sufficient quality to permit a judgment about the presence or absence of pericardial effusion and they were excluded from the study. In the remaining 33 patients the echocardiograms were of adequate quality to allow a diagnosis of pericardial effusion to be made or excluded. But an assessment of ventricular function was not possible in all, since many were seriously ill, not fully cooperative and/or were studied using the Polaroid photography technique. For this reason we have not included ventricular dimension measurements in this study.

Radiologists with no knowledge of the echocardiographic findings evaluated the chest X-rays, which were considered to show cardiomegaly if the cardiothoracic ratio exceeded 1:2 (fig. 4).

Electrocardiograms were examined for the presence of low voltage which was diagnosed if the voltage in standard leads I, II and III did not exceed 5 mm (0.5 mv) in any of these leads.

Serum thyroxine was determined by competitive protein binding and TSH by radioimmunoassay. Normal values for serum thyroxine are 4–11 μg/dl and for TSH 2–16 μU/ml.

Results

Echocardiography

Ten of the 33 patients (30%) had echocardiograms which were considered definitely positive for pericardial effusion, showing epicardial-pericardial separation during systole and diastole and a flat or minimally

Figure 1

An echocardiogram negative for pericardial effusion. A single moving pericardial echo is seen at low sensititity; at higher sensitivity the left ventricular posterior wall is visualised. There is no echo-free space between the epicardium (Epi) and pericardium (Peri). AW = anterior wall, IVS = interventricular septum, MV = mitral valve, Endo = endocardium.
moving pericardium. Of these, three were considered to have large effusions (greater than 200 cc) by our criteria. The ages of the patients with positive studies, 34–68 (mean 55) years, was not different from the group with negative echoes, 19–73 (mean 54) years. With the exception of one man who developed hypothyroidism and congestive heart failure while receiving corticosteroid therapy for Graves' ophthalmopathy, all patients with evidence of pericardial effusion had histories of untreated hypothyroidism for more than one year.

Chest X-ray

Thirteen patients had cardiomegaly on chest X-ray. Three of the ten patients with pericardial effusion on echo had no cardiac enlargement on X-ray. None of these three showed large echo effusions; all three with large echo effusions did have cardiomegaly. Five of the 13 patients with radiologic cardiac enlargement had negative ultrasonic studies (fig. 4).

Electrocardiogram

Low voltage was present in ten patients, five of the ten patients with positive echocardiograms and five of the 23 patients with negative studies. The heart rate, measured from the ECG, was significantly \( P < 0.05 \) slower in the group with positive (53 ± 8 beats/min) than with negative (68 ± 2 beats/min) echocardiograms (fig. 5).

Thyroid Function Studies

The concentration of serum thyroxine was 1.8 ± 0.3 \( \mu g/dl \) in the group with evidence of pericardial effusion and 1.5 ± 0.1 \( \mu g/dl \) in the group without effusion (fig. 5). Likewise, serum levels of TSH were not different in the two groups: 34 ± 4 U/ml and 38 ± 5 \( \mu U/ml \) in the positive and negative groups, respectively (fig. 5).

Follow-up Studies

Seven of the patients whose initial echocardiograms demonstrated pericardial effusion were re-studied after periods of thyroxine replacement therapy ranging from six months to two years. All patients were clinically euthyroid with normal serum thyroxine concentrations and all had negative echo-

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**Figure 2**

An echocardiogram showing the classic features of a large pericardial effusion: a flat pericardium, a large posterior echo-free space and a smaller anterior echo-free space. PE = pericardial effusion.
cardiograms on re-examination. Two of the patients who had resolution of echocardiographic evidence of pericardial effusion continued to have evidence of cardiomegaly on chest X-ray; in neither had the initial pericardial effusion been considered to be large.

Discussion

Cardiac enlargement, reduced cardiac pulsations and low electrocardiographic voltage was first associated with myxedema by Zondek. The resemblance of this clinical picture to pericardial effusion soon became evident. Based on successful pericardiocentesis in four hypothyroid patients with cardiomegaly on X-ray and a review of numerous individual case reports, Kern concluded that pericardial effusion was "a constant, early and major factor" in myxedema heart disease. More recent studies have been inconclusive. Kurtzman et al. diagnosed pericardial effusion by carbon dioxide angiography in seven of nine myxedematous patients with enlarged hearts, and Kitteredge et al. reported two similar cases in which the diagnosis was established by angiocardiographic dye injection. On the other hand, Watanakunakom et al. reviewed 400 cases of myxedema and found only two incidences of pericardial effusion.

Our study showed that a definite pericardial effusion could be demonstrated by echocardiography in

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**Figure 3**

An equivocal echocardiogram, showing a small epicardial-pericardial separation in systole and early diastole. The epicardial and pericardial echoes merge in mid-diastole, and the pericardial echo is not flat. Such recordings were classified as negative for pericardial effusion in this study (see text). Ch = chordae tendineae.

**Figure 4**

Marked cardiomegaly on chest X-ray in a myxedematous patient whose echocardiogram showed no pericardial effusion.
PERICARDIAL EFFUSION IN MYXEDEMA

Heart rate, serum thyroxine and TSH levels in patients with and without pericardial effusion. P = unpaired comparison of effusion vs no effusion groups. Brackets indicate standard error. N = 10 patients in the effusion group and 23 patients in the no effusion group.

Figure 5

Heart rate, serum thyroxine and TSH levels in patients with and without pericardial effusion. P = unpaired comparison of effusion vs no effusion groups. Brackets indicate standard error. N = 10 patients in the effusion group and 23 patients in the no effusion group.

ten of 33 (30%) of myxedematous patients. Of these, three were considered by our criteria to be large (> 200 cc) effusions. However, it is possible that the patients who came to our attention were a somewhat biased group favoring severely affected individuals. All but one of the group with positive echo studies had been hypothyroid for more than one year. It should be noted, however, that eight of the 22 patients with negative examinations also had longstanding myxedema. We were unable to demonstrate any significant difference in serum levels of thyroxine and TSH in the patients with and without effusion. The heart rate of the group with pericardial effusion was significantly slower than in the group with negative echoes.

Cardiomegaly on chest X-ray tended to be associated with echo-detected pericardial effusion, but a 30% (three out of ten patients) false negative rate and a 38% (five of 13 patients) false positive rate limited the diagnostic usefulness of radiographic assessments. Low voltage on ECG was equally non-specific (present in five of 23 noneffusion patients) and even less sensitive (present in only five of ten effusion patients) as an indicator of pericardial effusion. Reliance on these traditional methods of demonstrating pericardial effusion may result in an incorrect diagnosis.

None of the ten patients with echo-detected pericardial effusion developed cardiac tamponade, and no pericardiocentesis was performed. This is consistent with previous studies which noted the absence of hemodynamic consequences of myxedematous pericardial effusions; slow fluid accumulation and pericardial distensibility have been advanced as an explanation. Thus even large pericardial effusions in myxedema are generally not clinically significant in terms of hemodynamic cardiac embarrassment. However, the finding of cardiomegaly on chest X-ray always raises the differential diagnosis of pericardial effusion vs cardiac dilatation due to myocardial and/or coronary disease. Echocardiography is quite useful in resolving this question by demonstrating the presence or absence of a pericardial effusion.

Thyroxine replacement therapy in doses sufficient to render the patients euthyroid was successful in abolishing the effusions in all seven patients who were restudied. Previous authors have reported similar experiences. The unreliability of the chest X-ray is again shown by the two patients in whom cardiomegaly persisted despite disappearance of the effusion. Both these patients had evidence of old myocardial infarction in ECG, and one had hypertension with left ventricular hypertrophy.

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