Idiopathic Myocardiopathy of the Puerperium
(Postpartal Heart Disease)

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Victor J. Ferrans, M.D., Ph.D., and Richard G. Hibbs, Ph.D.

For more than a century physicians1 have been aware of the clinical syndrome of postpartal nonvalvular myocardial disease of unknown origin. Sporadically cases have been reported and various etiologic theories proposed, but the relative rarity of this disease and inconsistent and incomplete descriptions have rendered difficult its understanding. Not the least of the problems is the lack of a universally accepted definition of the syndrome.2 There is little wonder that its very existence is disputed.3, 4

This report relates our experience with 15 patients with postpartal heart disease. The presentation is qualified by the fact that the distribution of our patients is probably skewed toward the more seriously ill category, since mild cases may not have been recognized or may not have been referred for hospitalization.

Criteria for admission to our study consisted of (1) absence of the history, symptoms, and physical findings of heart disease prior to the puerperium, (2) appearance of signs and symptoms of heart disease between the first and twentieth week of the puerperium, and (3) inability to establish an etiologic basis for the heart disease. The 1-week interval between delivery and admission to the study was chosen to eliminate patients who developed mild heart failure during delivery that was not recognized for several days as well as those with possible pre-existing cardiac diseases that became clinically recognizable during pregnancy.

Demography

The essential statistics of the group are presented in table 1. All patients are Negro, in keeping with our own previous experiences and with reported cases. This syndrome appears earlier in the female patients than does idiopathic myocardial disease in male patients. All patients were housewives, although most had worked for brief periods as household servants.

History

One half of the patients reported heart disease, which was hypertensive or arteriosclerotic in origin in one or both parents. This high rate of familial heart disease in such relatively young patients raises the possibility of hereditary susceptibility to cardiovascular disease.

Two patients recalled an uncomplicated respiratory infection prior to the onset of symptoms of congestive heart failure but had not had appropriate diagnostic tests. Although some type of post-infectious myocardiopathy is possible, this finding in two patients is of doubtful significance.

Although our patients come from a socioeconomic group which characteristically suffers from inadequate nutrition, the nutritional background of the patients was extremely deficient, particularly in conjunction with the numerous, frequently almost sequential pregnancies in the long duration of the malnutrition. Of 15 patients, only three gave histories of adequate nutrition for extended periods. Dietary habits of the remainder were never better than borderline, and then only during brief periods of affluence. As a rule breakfast consisted of coffee or soda pop, hominy grits being taken on one or two mornings each week. Lunch was omitted or

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Table 1
Age and Race of Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>19 or less</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49*</th>
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<tbody>
<tr>
<td>White</td>
<td>—</td>
<td>8</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Negro</td>
<td>1</td>
<td>8</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>8</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

*One patient aged 40, one patient aged 41.

disease. Nine patients were said to experience one of these complications during the pregnancy immediately preceding onset of the cardiac disease. In many instances hospital records were not available. The incidence and significance of "toxemia" is uncertain, for in at least 10 pregnancies delivery was effected by midwife at home. In other instances, the terms "toxemia" and "preeclampsia" were used by various physicians with differing criteria of these entities. Thus, no estimate can be made of the true incidence and nature of "toxemia" or "preeclampsia" in the 68 pregnancies, although by history 28 were associated with this complication. It seems likely that in only one instance did true eclampsia of pregnancy occur. Only two of the 15 patients noted onset of heart disease following the first pregnancy, whereas eight patients experienced this phenomenon after the second or third gestation (table 2). Three patients developed heart disease after the fifth pregnancy.

Orthopnea, paroxysmal nocturnal dyspnea, exertional dyspnea, edema, and cough were experienced by practically all patients during the evolution of their illness (table 3). Invariably the initial appearance of left heart failure was followed at various intervals by symptoms of right heart failure. Of seven patients with chest pain or hemoptysis, six had subsequent clinical or autopsy evidence of pulmonary embolism. Prolonged bedrest did not predispose to thromboembolic phenomena in any of the patients studied.

Of interest was the high incidence of colicky, severe, persistent abdominal pain. With return of cardiac compensation and recession in hepatomegaly, these symptoms generally subsided, although they tended to persist to a mild degree for many months without demonstrable congestive heart failure.

Table 2
Number of Pregnancies at Onset of Myocarditis

<table>
<thead>
<tr>
<th>Pregnancy at onset</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
or intrinsic gastrointestinal disease. The frequency of palpitation and cough was greater than usually encountered in congestive heart failure.

Not all patients were seen during the earlier phases of illness. The physical findings recorded in table 4 are in part based on hospital records and depend on the variable acuity and reliability of several observers. Cardiomegaly, diastolic gallop rhythm, accentuation of the second pulmonic sound, hepatomegaly, venous distention, bilateral basal crepitant rales, and pedal edema were characteristic. As a rule ascites was not present during earlier phases of the initial episode of cardiac insufficiency. Premature ventricular contractions were noted in one third of the patients at the time of admission to the hospital and in practically all patients at some time during their illness. The systolic murmur, present in nine patients, was characterized as precordial, blowing, radiating slightly into the axilla and of grade I or II intensity. The first heart sound was of decreased intensity and “muffled” character in most patients.

### Laboratory Studies

**Hematology**

Hemoglobin electrophoresis performed in 12 of the patients revealed nine subjects with type-A hemoglobin, two patients with AC, and one with AS hemoglobin. Of three additional patients who died before typing, one had a positive sickle-cell preparation.

Blood groupings were determined in 10 patients. All were Rh positive. There were six with type O, two with type A, and one each with types AB and B.

Although all patients had total and differential leukocyte counts well within normal limits, seven had hypochromic, microcytic anemia that ultimately responded to treatment with iron and a good diet. Erythrocyte sedimentation rates were normal in 11 of 14 patients; in two, the value was increased for no apparent cause; in one, secondary syphilis was present. Of the other 14 patients, one had a positive serologic test for syphilis, a residue of previous, adequately treated, latent syphilis. All patients had a negative response to multiple lupus erythematosus preparations. C-reactive protein and anti-streptolysin-O titers were determined at least once in 10 patients and were within normal limits with one exception, a one plus C-reactive protein for which no cause could be determined.

Total serum cholesterol was measured in 13 of the 15 patients. In six patients serum cholesterol levels were above 250 mg. per 100 ml., the upper limit of normal in our laboratory. One of these subsequently manifested mild diabetes mellitus. Furthermore, 12 of the 13 patients had values above 220 mg. per 100 ml. Because of the small size of the group it is impossible to draw valid conclusions.

### Liver Function

Unlike the other tests, tests of liver  

<table>
<thead>
<tr>
<th>Signs</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiomegaly</td>
<td>100</td>
</tr>
<tr>
<td>Accentuation $P_2$</td>
<td>93</td>
</tr>
<tr>
<td>Protodiastolic gallop rhythm</td>
<td>67</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>67</td>
</tr>
<tr>
<td>Edema</td>
<td>60</td>
</tr>
<tr>
<td>Venous distention</td>
<td>60</td>
</tr>
<tr>
<td>Pulmonary basal fine rales</td>
<td>60</td>
</tr>
<tr>
<td>Systolic mitral murmur</td>
<td>60</td>
</tr>
<tr>
<td>Ascites</td>
<td>47</td>
</tr>
<tr>
<td>Premature contractions</td>
<td>33</td>
</tr>
</tbody>
</table>

### Table 3

**Incidence of Symptoms**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percentage of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopnea</td>
<td>100</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>100</td>
</tr>
<tr>
<td>Exertional dyspnea</td>
<td>94</td>
</tr>
<tr>
<td>Edema</td>
<td>94</td>
</tr>
<tr>
<td>Cough</td>
<td>88</td>
</tr>
<tr>
<td>Weakness</td>
<td>69</td>
</tr>
<tr>
<td>Ascites</td>
<td>63</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>50</td>
</tr>
<tr>
<td>Palpitation</td>
<td>50</td>
</tr>
<tr>
<td>Chest pain</td>
<td>25</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>25</td>
</tr>
</tbody>
</table>
function were performed on many patients late in the course of illness rather than during the earliest stages of cardiac disease. Thereafter repeated studies were done.

Bromsulphalein excretion was measured serially in 13 patients. Five subjects, studied after all evidence of congestive heart failure had disappeared, excreted the dye normally. Bromsulphalein retention in the remaining eight ranged from 10 to 70 per cent and averaged 38 per cent (median 42 per cent). The latter patients had been in congestive heart failure for prolonged periods and were more seriously ill than those with normal dye excretion. Five of the patients with marked retention of dye failed to regain normal hepatic excretory function and eventually died of heart disease.

**Total Serum Proteins**

The total serum protein was within normal limits in 13 subjects, borderline in one, and in one was 9.6 Gm. per cent with an albumin/globulin ratio of 1. After prolonged hospitalization both values became normal. In several patients the albumin/globulin ratios were barely within the lowest limits of normal. With hospitalization the level of serum albumin and total protein generally increased to more definitely normal values. Electrophoresis of serum proteins was performed in 11 of the 15 patients on one or more occasions. One patient early in the clinical course exhibited a 20-per cent reduction in albumin and a 50-per cent increase in globulin. Subsequent examination after several years of apparent health revealed only a questionable increase in serum globulin.

**Renal Function**

Routine urinalysis on admission to our study revealed a trace to one plus albuminuria in half of the patients, most of whom were in congestive heart failure. Thereafter, renal function was measured at intervals. Our initial plan to perform these tests after recovery from congestive heart failure was modified because of inability to effect complete compensation in some patients. In some instances, specific tests of urinary function were not feasible. Seven patients with abnormally low renal concentrating ability on specific testing or casual urine examination, failed to exhibit decrease in heart size; six eventually died of heart disease. Of eight patients with normal renal concentrating ability, four showed return to normal heart size (one of these suffered a fatal relapse), two died, and two exhibited some decrease in heart size.

**Roentgenography**

Serial thoracic teleroentgenograms with barium in the esophagus in all patients initially showed generalized cardiomegaly involving all chambers. In five patients a double shadow ascribable to left atrial enlargement was noted on posteroanterior views of the chest (fig. 1).

**Electrocardiography**

All patients had electrocardiographic changes consistent with left ventricular hypertrophy (fig. 2). Conduction defects were not observed. Rhythm disturbances were transitory and limited to bigeminy, trigeminy, and multiple unifocal and multifocal premature ventricular contractions, disappearing at times with discontinuation of digitalis and supplementation of potassium intake. One patient with recurrent pulmonary embolization developed large P waves and QRS changes consistent with right ventricular hypertrophy.

**Gastrointestinal Function**

I$^{131}$-labeled triolein uptake, determined in nine of the patients, was within normal limits.

**Pulmonary Function**

Ventilatory studies were completed in four patients with cardiomegaly. In two patients persistent congestive heart failure resulted in moderate decrease in vital and maximal breathing capacities; in the other two values were normal.

**Treatment**

As previously described, these patients were maintained on prolonged, complete, bed
rest, for periods in excess of 1 year in some instances, or until the heart had returned to normal size. Measures included bedside commode, air-conditioning, bedside nursing care, television, radio, and occupational therapy.

As expected, there were breaches in discipline and occasional personal problems requiring rare, brief absences from the hospital.

Another departure was the use of mercurial instead of thiazide diuretics, because of prior
experience with more conventional heart diseases that showed potassium-wasting effect of thiazide compounds and intolerance to digitalis. Digitalis was used, however, in our patients. All of our 15 patients exhibited what was considered to be somewhat unusual susceptibility to digitalis with a propensity to multiple multifocal premature ventricular contractions. The daily digitalis dosage was individualized for the first few months of hospitalization in each patient. With improvement the problem generally disappeared, but it persisted in patients who did not show clinical improvement. All patients empirically received potassium chloride in liquid form.

**Hospital Course**

Initially symptoms of congestive failure disappeared, usually after a few weeks of bedrest. The physical signs of congestive heart failure were somewhat slower to respond, persisting for several weeks after the patient had become symptom-free. Excepting cardiomegaly, the last of the physical abnormalities to disappear was the protodiastolic gallop rhythm. In some patients it persisted for many months. When diminution in heart size occurred, it was a slow process often not perceptible even at monthly intervals.

Of 15 patients, nine have died. Four died within a month of admission to the series; three of them were admitted in severe congestive heart failure and remained so until death. The fourth patient, with cardiomegaly but without cardiac insufficiency, left the hospital contrary to advice 2 weeks after admission and died suddenly at home 10 days later.

Of the remaining five fatalities, four patients had been continuously hospitalized 12 to 14 months without marked reduction of heart size. Three of these patients im-

**Figure 2**

Left. Admission electrocardiogram of a 27-year-old Negro woman showing inverted precordial T-wave changes and voltage suggestive of left ventricular hypertrophy. Right. Same patient 24 months later (no cardiomegaly on x-ray). T-wave changes persist.
proved sufficiently to return to outpatient status but eventually succumbed. The fourth patient never left the hospital. The last fatality occurred in a patient who, during initial hospitalization, became symptom-free with return of normal heart size over a 12-month period. After return to outpatient status and a regimen of moderate activity she remained asymptomatic for 8 months. Thereafter, she embarked on a program of a 16-hour workday coupled with grossly inadequate nutrition. After 2 months of recurring symptoms of congestive heart failure, she developed acute pyelonephritis and died in intractable congestive heart failure despite an additional 3 months of intensive hospital care. This recurrence of cardiac difficulties was due to failure to heed medical advice. The mortality rate (60 per cent) is at variance with that reported in the literature but in keeping with our previous experiences.

Of the six survivors, three became symptom-free and experienced return of heart size to normal after 6, 6, and 14 months of hospitalization, respectively. The other three patients showed marked clinical improvement and definite but limited decrease in heart size over 12 months or more of hospitalization and are being observed as outpatients.

Complications

Thromboembolism

Next to digitalis toxicity, the most frequently encountered complication was pulmonary thromboembolism, which occurred in six patients, two of whom suffered from concurrent thrombophlebitis of a lower extremity. There were associated cerebral emboli in two patients. In every instance the initiation of thromboembolic phenomena preceded admission to the study group and was not made worse by prolonged bedrest.

Bronchopneumonia

Bronchopneumonia occurred as a terminal complication of intractable heart failure in several patients.

Acute Pyelonephritis

This complication was of considerable sig-

nificance in two of three patients in whom it occurred. The first of these showed progressive decrease in cardiomegaly during the early portion of initial hospitalization. Incident to acute pyelonephritis associated with hypertension approximating 150 to 170/100 to 110 mm. Hg, her heart rapidly enlarged, almost to initial size. After control of infection and return of blood pressure to normal, the heart size gradually decreased to normal. Renal function was normal. In view of her labile blood pressure and the untoward response to transitory hypertension she has been maintained on reserpine. There have been no additional episodes of renal infection nor of hypertension.

The second patient, described previously, experienced return of heart size to normal during initial hospitalization but relapsed amid circumstances which included poor nutrition and a 16-hour workday. On terminal hospitalization she was uremic, hypertensive (180/120) with acute pyelonephritis, cardiomegaly, and cardiac insufficiency. Autopsy revealed chronic pyelonephritis.

The third patient experienced two episodes of acute pyelonephritis during observation. Neither affected heart size or blood pressure. However, this patient showed no decrease in cardiomegaly in spite of 18 months of complete bed rest. Postmortem examination failed to reveal evidence of renal disease.

One of the patients who died had reported a single episode of pyelonephritis 10 years previously and had persistent pyuria and minimal albuminuria during her sole 10-day hospitalization. No autopsy was performed. Another patient who suddenly died after terminating a brief hospitalization by desertion was noted to have pyuria and bacteriuria at the time of departure. Finally, the sixth patient to present any suggestion of renal abnormalities had never experienced clinical kidney disease but autopsy disclosed calcium-containing casts and inflammatory cells in the renal tubules. She had not shown a decrease in heart size with prolonged bed rest.

Cardiac Irregularities

Except for atrial and ventricular premature
contractions, the only arrhythmia was transitory atrial fibrillation appearing during gynecologic surgery under spinal anesthesia in a patient whose heart had returned to normal size. There have been no recurrences of arrhythmia.

Pregnancies

Subsequent to their initial episode of postpartal heart disease six patients have had a total of six full-term pregnancies, at least two of which were complicated by the appearance of congestive heart failure in spite of digitalis. After all six pregnancies, cardiac insufficiency became worse postpartum. Moreover these six patients experienced four additional pregnancies that did not go to term. Existing congestive heart failure may have become more severe following abortion of a 3-month fetus. The remaining three pregnancies, terminating at 6, 6, and 7 months, respectively, were neither complicated by congestive heart failure nor followed by recurrence of the postpartal cardiac syndrome.

Natural Course of the Disease

According to our experiences the typical patient with postpartal heart disease is a young multiparous Negro with long-standing marginal or inadequate nutrition and about a 50-to-50 chance of having a history of “toxemia” incident to previous pregnancy or to that pregnancy immediately following which heart disease appeared. Between one and 20 weeks following uneventful delivery she experiences the rather rapid onset of symptoms of left ventricular failure. As a rule she delays hospitalization for 1 or 2 weeks in spite of the severity of her symptoms, and commonly develops signs and symptoms of right ventricular failure prior to hospitalization. Initial response to treatment is good and rather prompt with the exception of persistence of cardiomegaly. A sizable minority of these patients experience thromboembolic phenomena. Treatment is complicated by sensitivity to digitalis preparations and by frequently persistent vague abdominal discomfort. Symptomatic response to treatment is so complete that she usually insists on leaving the hospital.

Congestive heart failure may recur with subsequent pregnancy and almost certainly follows full-term delivery. Intercurrent pyelonephritis, discontinuation of digitalis, and possibly resumption of poor dietary habits and undue physical exertion may cause relapse. The subsequent course is characterized by frequent exacerbations requiring hospitalization and may be associated with thromboembolic phenomena. Cardiomegaly persists and eventually increases. The possibility of sudden death remains constant.

If the patient remains at prolonged bedrest during the acute episode until maximal benefits have been achieved, she stands a good chance of experiencing a return of heart size to normal. This does not guarantee future immunity from relapse, particularly if diet, and living and working habits are not ideal. Follow-up care is extremely important.

The life span of nine patients who died averaged 29 months following onset of heart disease, the range being 4 to 58 months. The six remaining patients have survived for an average of 71 months (range 24 to 129 months) since the first signs of heart disease.

Postmortem Findings

Postmortem examination was performed in five of nine fatal cases. With exception of rare incidental findings, e.g., cholelithiasis, cervicitis, etc., abnormalities were limited to those arising directly or indirectly from cardiorenal disease.

Heart

Grossly the heart was pale and flabby in all but one instance. Heart weight varied from 465 to 600 Gm., the average being 527 Gm. In three patients there were rare old fibrinous epicardial patches or minimal adhesions, otherwise the pericardium was normal. One patient had a clear pericardial effusion approximating 500 ml. The coronary arterial system was completely patent in all and free from atheromatous change except for scattered minimal atheromatous plaques in one.

Maximal left ventricular thickness varied

Circulation, Volume XXXII, July 1965
from 4 to 21 mm., averaging 11 mm. (median 14). Measurements of the right ventricle ranged from 2 to 8 mm., averaging 5.4 mm. (median 6 mm.). Circumferential valvular measurements were within upper normal limits. Both valvular and mural measurements are subject to the usual limitations of marked cardiac dilatation. The valves appeared normal.

Grossly the endocardial surface appeared normal in two of the five subjects. In the others there were numerous gray-white patches of endocardial thickening, most marked in the left ventricle but present in two instances in the right ventricle with additional uniform gray thickening of the left atrial endocardium. The plaques involved both free and septal walls of the ventricles, were more prominent in the apical portions, were 2 to 3 mm. thick, and did not involve the myocardium. Patches varied from 0.5 to 4 cm. in diameter and were usually associated with minimal thickening of the chordae tendineae, apparently by the same process. One large plaque, on the septal wall of the left ventricle, exhibited extensive calcification. This was in the patient who exhibited some coronary and aortic atherosclerosis. She was the only subject to present evidence of sclerotic changes in the pulmonary circulation and had developed pulmonary heart disease attributable to recurrent pulmonary embolization. In one patient mural thrombi (two) were noted at sites of left ventricular endocardial thickening.

Microscopic examination of hearts with PAS and with hematoxylin and eosin staining technics was performed. Neither amyloid nor PAS-positive material was noted. Interstitial edema and scattered areas of perivascular and interstitial infiltration by inflammatory cells were present in all subjects (fig. 3). Generally this was unimpressive, consisting largely of lymphocytes, although histiocytes and polymorphonuclear leukocytes were often present. Scattered areas of fatty infiltration were noted in three patients. Dispersed throughout the myocardium of each patient were variable areas of interstitial fibrosis and areas of muscle degeneration (fig. 4). The latter were characterized by many bizarre or pyknotic nuclei with pleomorphic hyperchromatism as well as muscle fibers that had lost their striation and nuclei and appeared to be undergoing hyaline degeneration. Endocardial thickening, present in four patients, was minimal to marked (fig. 5) and showed scattered limited infiltration by chronic inflammatory cells in two. Beneath the thickened endocardium of one patient hemorrhage and necrosis were noted, whereas moderate fatty infiltration had occurred in the same location in another of the autopsied patients. In the thickened endocardium and the fibrotic infiltrations of the myocardium the elas-
tic-tissue content correlated directly with the fibrous-tissue content.

All patients exhibited severe chronic passive congestion of the lungs and of intraabdominal organs. Pulmonary infarction of recent origin was noted (two patients) as well as evidence of old infarction (one patient). Four of the five had chronic passive congestion of the liver with central lobular necrosis. Massive chronic passive congestion and atrophy were noted in the fifth patient. With the exception of chronic bilateral pyelonephritis in one subject there was no postmortem evidence of renal disease.

At autopsy several blocks of tissue were obtained from each of the four chambers of the heart and from the interventricular septum. The blocks were frozen rapidly, mounted, and sectioned without prior fixation at a thickness of 6 microns in a cryostat.

Individual sections were fixed, whenever indicated, with 4-per cent formaldehyde. Preliminary study showed that slightly better morphology could be obtained when the tissues were fixed before sectioning. It seemed desirable, however, to integrate the histochemical pattern of specific areas of the tissue, which could be best accomplished by the use of serial sections examined by the methods described below. This excluded the use of block fixation which would interfere seriously with enzyme technics.

The following histochemical technics were performed: study of tissue autofluorescence in unfixed, unstained sections, for estimation of the amount of lipofuscin present8 and for identification of elastic-tissue fibers; phase-contrast microscopy in unfixed and in formalin-fixed sections for details of fine tissue morphology and for orientation purposes in sections stained by other methods.

The histochemical methods included the following: PAS reaction; cresyl-violet staining for metachromasia and for identification of tissue mast cells; Sudan black9 and Nile-blue sulfate7 staining for lipids; fluorescent lipid stains (benzpyrene8 and phosphine9); plasmal reaction for plasmalogens10; alkaline phosphatase;11 acid phosphatase,12 esterase,13 cytochrome oxidase;14 and succinic dehydrogenase.15 Controls for the lipid stains were done by extracting unfixed sections prior to staining with chloroform-methanol, 2/1, v/v.10

Preparations were examined with a Reichert Zetopan microscope equipped with optics for bright-field, phase-contrast, and fluorescence microscopy. Fluorescence photomicrographs were taken on 35 mm. high-speed Ektachrome film, daylight type.

Comparisons were made with histochemical patterns of normal human and animal hearts, and with hearts of patients with alcoholic cardiomyopathy. Allowances were made for time elapsed since death according to a pilot study conducted with human and animal hearts.16

All hearts demonstrated similar histochemical changes, differences being quantitative only, so that individual findings need not be reported separately. Microscopically there was much variation in fiber size; edematous and partially hyalinized fibers were interspersed irregularly. Variable areas of fibrosis were seen throughout. Changes were most marked in the ventricles but were present in the atria. The presence of inflammatory cells was highly variable.

The amount of lipofuscin was within normal limits for the age of these patients. Lipofuscin granules were easily identified by their

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Figure 5
Area of myocardium and endocardium showing endocardial thickening and calcification, infiltration by inflammatory cells, and myocardial fibrosis and degeneration. Hematoxylin-eosin stain; × 50.

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Circulation, Volume XXXII, July 1965
brownish color and by their characteristic golden-yellow autofluorescence. Nile-blue sulfate and Sudan dyes stained these granules even after prolonged extraction with lipid solvents. The esterase and acid phosphatase reactions were positive in these granules, whereas the alkaline phosphatase reaction was negative. Capillaries were the only myocardial structures stained by the alkaline phosphatase reaction. Lipofuscin granules failed to stain by the succinic dehydrogenase and cytochrome oxidase reactions.

With a cresyl violet stain the number of mast cells was normal. No metachromasia was found.

The periodic-acid-Schiff reaction was within normal limits. Accumulations of PAS-positive material, reported in some cases of familial cardiomegaly,17–19 could not be demonstrated.

The fluorescent stains for lipids in this study are considerably more sensitive than the ordinarily used Sudan dyes.16 This made possible identification of very small lipid droplets sometimes seen between mitochondria in interfibrillar spaces of the cardiac fibers.

Benzpyrene stained well all lipid-containing structures of cardiac muscle, including mitochondria and intercalated discs (fig. 6) whereas phosphine stained mostly neutral lipids. There was little fatty change except in areas with heavy deposition of relatively large fat droplets. Such areas corresponded to those with diminished or absent succinic dehydrogenase and cytochrome oxidase activity. We interpreted these changes as evidence of mitochondrial damage with resulting impairment of oxidation of lipids which therefore accumulate. Lipid in the droplets was identified as triglyceride by paper chromatographic analysis of the lipids extracted from cryostat sections from involved areas. Occasional lipid-laden macrophages were observed in these areas. The changes were in sharp contrast to those observed in hearts of patients with alcoholic cardiomyopathy (fig. 7) which showed heavy, diffuse deposition of minute fat droplets throughout, along with focal areas of more pronounced fatty change. Smaller fat droplets could not be clearly stained with the Sudan dyes, but were easily demonstrated by fluorescence technics.

Plasmal reaction was localized in the mitochondria between myofibrils and at the poles of nuclei, in interfibrillar spaces and intercalated discs. Fat droplets, myofibrils, and lipofuscin granules were negative. Intensity of staining was the same in larger, hypertrophic fibers as in smaller, more normal ones. Areas of fatty change showed from moderate to marked decrease in intensity of the plasmal reaction.

Succinic dehydrogenase and cytochrome oxidase reactions were localized to mito-

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**Figure 6**

Left ventricular myocardium. Note interstitial fibrosis. Fatty change is absent. Benzpyrene stain; × 200.

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**Figure 7**

Left ventricular myocardium from patient with alcoholic heart disease illustrating the very pronounced, diffuse deposition of neutral lipid droplets. Compare with figure 6. Benzpyrene stain; × 200.
A focal area of myocardial necrosis with loss of enzymatic activity. Cytochrome oxidase stain; ×100.

Figure 8

Chondria of muscle fibers (fig. 8). Faint reactions were observed in some inflammatory cells. Sharpness of localization was variable, due to postmortem changes which affect the mitochondria rapidly, so that only limited conclusions can be drawn. In general, intensity of reaction was somewhat decreased when compared to normal hearts in similar circumstances of postmortem autolysis (fig. 9). There were spotty zones of varying degrees of lessened activity with some fibers almost completely negative. In this respect the succinic dehydrogenase reaction seemed to be a more sensitive indicator of cell damage than the cytochrome oxidase reaction. During this work it became obvious that the succinic dehydrogenase reaction provided a better index of myocardial cellular damage than the other histochemical procedures used. Areas of damage corresponded to those of fatty change and decreased plasmal reaction. There were individual fibers, however, with diminished succinic dehydrogenase reaction and no lipid droplets as well as others with normal enzymatic reactions and small lipid droplets. All fibers containing large fat droplets demonstrated a very reduced response for both oxidative enzymes.

These changes were strikingly different from those seen in alcoholic myocardopathy, in which there was diffuse and pronounced decrease of succinic dehydrogenase activity throughout (fig. 10). We wish to emphasize that on routine histologic examination the two groups of patients could not be separated, whereas they were readily differentiated by histochemical studies.

Summary

It should be clearly understood that no evidence was uncovered to indicate an unequivocal etiology for this uncommon disease. One is tempted to qualify "uncommon" in that it no longer connotes the same extreme degree of rarity that would appear from medical literature. Over the same period that these cases were collected an equal number were recognized but unavailable for study for various reasons.

Figure 9

Section from normal human heart showing the normal pattern of staining for succinic dehydrogenase; ×500.

Figure 10

Patient with alcoholic myocardopathy. A marked decrease in the intensity of the reaction is evident throughout. Succinic dehydrogenase technic; ×500.
POSTPARTAL HEART DISEASE

Unfortunately, the size of our series precludes statistical analysis. The apparent tendencies to hypercholesteremia, blood-group predilection, and increased incidence of abnormal hemoglobin types are in need of further exploration. One would be remiss not to note at this point that at least one report related several instances of familial incidence of postpartal heart disease.

We are more certain of the significance of malnutrition as a factor in the genesis of this syndrome, although we are unable to assign a precise role. Similarly, the deleterious effects on such patients of hypertension, pyelonephritis, and full-term pregnancy have impressed us, although we can make no judgment as to their frequency of occurrence. Probably, as so often happens, we are most certain of our single pre-investigatory premise that postpartal heart disease is a serious and pernicious syndrome, quite different from that described in most of the literature. That prolonged bed rest is not a panacea is obvious. It is of sufficient merit, however, to warrant use in all such patients, for periods up to 1 year at least.

References