# CASE REPORTS

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# Cardiovascular Complications During Prolonged Starvation

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PROLONGED STARVATION is an extreme and effective treatment of obesity.[1] In otherwise healthy persons, cardiovascular complications of this treatment have rarely been reported.[2,3,15] Recently a number of cardiac deaths have been associated with fasting modified by liquid protein supplementation.[4,5] We report a case of severe cardiovascular complications that occurred during a prolonged fast unmodified by protein supplements. In this case, endomyocardial biopsy specimens were obtained, and examination of them showed striking pathological findings.

## Report of a Case

A 26-year-old woman lawyer whose weight was 90 kg (198 pounds) and height 160 cm (5 ft, 3 in) began a self-imposed fast in September 1977. She first sought medical attention during the following month when she felt well except for a sensation of cold and occasional orthostatic dizziness. Her medical history included psychotherapy for depression. The medical history she gave was judged to be reliable, and she was not taking medications at the time of the fast. Findings on physical examination by one of the authors (M.R.) were normal except for obesity. The electrocardiogram (ECG) showed normal voltage with T wave inversions in $V_1$ and $V_2$ which were normal for her age. X-ray studies of the chest showed no abnormalities. Laboratory data are summarized in Table 1.

She made biweekly office visits and continued to feel well while taking nutritional supplements: potassium chloride (40 mEq per day), calcium lactate (1.8 grams per day) and multivitamins with folate (1 mg per day). She drank at least a quart of water a day. The serum potassium level varied between 3.0 mEq per liter and 5.4 mEq per liter. The serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) remained slightly elevated. The blood pressure, which had initially been 100/85 mm of mercury, dropped to 80 mm of mercury palpable without orthostatic changes or tachycardia. By January 1978, she weighed 62 kg (136 pounds) and was unwilling to break the fast despite recommendations that she do so. A week before admission to hospital she started a new job and became physically more active and increasingly fatigued.

On January 17, 1978, her psychiatrist sent her to the emergency room in a taxi because she felt profoundly weak. She denied specific complaints of shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, chest pain or palpitations. On arrival at the hospital she was alert, but blood pressure could not be obtained by cuff or by palpation. The pulse was 130 beats per minute and regular. She was afebrile. Skin turgor was normal and the mucous membranes were moist. The neck veins were full and visible 6 to 8 cm above the sternal angle. The lungs were clear and the heart sounds were distant. A summation gallop was present, and there were no murmurs or pericardial friction rub. The liver was palpable 3 cm below the right costal margin, with a 10- to 12-cm span by percussion, and was nontender and soft. There was no pedal edema and the extremities were cool and dry. Findings on neurological examination were normal.

### *Laboratory Findings*

Blood test findings on admission are summarized in Table 1 under the heading "After Four-Month Fast." X-ray films of the chest showed increased right perihilar markings and a normal

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heart size. The initial ECG (Figure 1) showed a supraventricular tachycardia with aberrant condition of the left bundle branch type (versus ventricular tachycardia) at 130 beats per minute. Two hours later the ECG (Figure 2) showed sinus tachycardia of 100 beats per minute, low voltage of the QRS complexes, prolonged QT interval of 0.40 seconds and absence of the bundle branch block. An echocardiogram (Figure 3) showed decreased septal motion and thickness with an enlarged left ventricular diastolic diameter (LVID) of 5.4 cm (LVID per sq m = 3.3, normal <3.2), enlarged right ventricular diastolic diameter (RVD) of 2.8 cm (RVD per sq m = 1.6, normal <1.4), and decreased velocity of circumferential shortening ($V_{cf}$) of 0.96 cm (normal >1.05). Arterial blood pH was 7.27, $P_{O_2}$ was 126 mm of mercury and $P_{CO_2}$ was 11 mm of mercury on 4 liters per minute of oxygen administered nasally.

*Treatment*

In the emergency room, the blood pressure became palpable at 50 mm of mercury after infusion of 1,000 ml of lactated Ringer solution. The patient was transferred to the coronary care unit and a central venous pressure catheter was placed with initial value of 14 cm of water. Digoxin was started but was discontinued after the appearance of sequential premature ventricular beats. On the second hospital day, a Swan-Ganz catheter was inserted. Initial right-sided heart pressures were as follows: right atrium, mean pressure 10 mm of mercury; right ventricle, 30/10 mm of mercury; pulmonary artery, 30/18 mm of mercury (mean,

TABLE 1.—*Laboratory Data for Fasting Patient*

| *Laboratory Test* | *Normal Values* | *After One-Month Fast* | *After Four-Month Fast* |
|---|---|---|---|
| Hematocrit | .... | 51 percent | 36 percent |
| White blood count | .... | 14,500 with normal differential | 6,300 with normal differential |
| Platelets | .... | Adequate | Adequate |
| Electrolytes | .... | Normal, except K = 3.6 mEq/L | Na = 138 mEq/L, K = 3.7 mEq/L, Cl = 103 mEq/L, and $CO_2$ = 3 mEq/L |
| Blood urea nitrogen (BUN) | .... | 3 mg/dl | 4 mg/dl |
| Uric acid | 4.0-8.5 mg/dl | 9.3 mg/dl | 6.7 mg/dl |
| Total protein | .... | 6.4 gm/dl | 5.1 gm/dl |
| Albumin | 3.9-5.7 gm/dl | 4.2 gm/dl | 3.1 gm/dl |
| Serum calcium | 8.7-10.5 mg/dl | 10.4 mg/dl | 7.5 mg/dl |
| Serum phosphorus | 2.4-4.6 mg/dl | 2.7 mg/dl | 3.6 mg/dl |
| Cholesterol | 140-225 mg/dl | 175 mg/dl | 155 mg/dl |
| Fasting blood glucose | 40-115 mg/dl | 87 mg/dl | 400 mg/dl (on IV solution) |
| Serum creatinine | 0.6-1.4 mg/dl | 1.2 mg/dl | 1.6 mg/dl |
| Total bilirubin | 0.1-1.4 mg/dl | 0.9 mg/dl | 2.2 mg/dl |
| Serum lactic dehydrogenase (LDH) | .... | 198 mU/ml (normal 60-225 mU/ml) | 350 mU/ml (normal 100-230 mU/ml) |
| Serum glutamic oxaloacetic transaminase (SGOT) | 0-41 mU/ml | 53 mU/ml | 160 mU/ml |
| Serum glutamic pyruvic transaminase (SGPT) | 1-45 mU/ml | 65 mU/ml | .... |
| Serum creatine phosphokinase (CPK) | 4-51 mU/ml | .... | 40 mU/ml (serial CPK-MB isoenzymes, less than 5%) |
| Serum magnesium | 1.8-3.0 mg/dl | .... | 2.1 mg/dl |
| Serum copper | 70-140 μg/dl | .... | 60 μg/dl |
| Serum cortisol (fasting) | 6-25 μg/dl | .... | 28 μg/dl |
| Thyroxine-RIA | 5.4-13.0 μg/dl | .... | 4.8 μg/dl |
| Thyroid-stimulating hormone (TSH) | <10 μU/ml | .... | 1.9 μU/ml |
| Serum folate | 4-16 ng/ml | .... | 4 ng/ml |
| Vitamin $B_{12}$ | 350-1,000 pg/ml | .... | 1,372 pg/ml |
| Urine ketones | .... | Large | Large |
| Blood cultures | .... | .... | Negative |
| Urine cultures | .... | .... | Negative |
| Sputum cultures | .... | .... | Negative |

24 mm), and pulmonary artery wedge (PAW), mean pressure 18 mm of mercury. Oximetry data showed a wide arteriovenous (AV) oxygen difference of 48 ml per liter (normal 30 to 40 ml per liter) and no evidence for an intracardiac shunt.

*Hospital Course*

For the first seven days, the mean PAW ranged from 12 to 24 mm of mercury and increased notably with small increments of intravenous fluids. The serum potassium levels were as low as 2.4 mEq per liter (day 5) and the serum phosphorus levels became as low at 1.0 mg per dl (day 5). The urine output did not exceed 20 ml per hour for the first nine days unless the patient was given intravenous furosemide in doses up to 200 mg. On the fifth day, the patient remained hypotensive and oliguric. She was willing to consume only small amounts of caloric liquids. On the fifth, sixth and seventh days, she was given

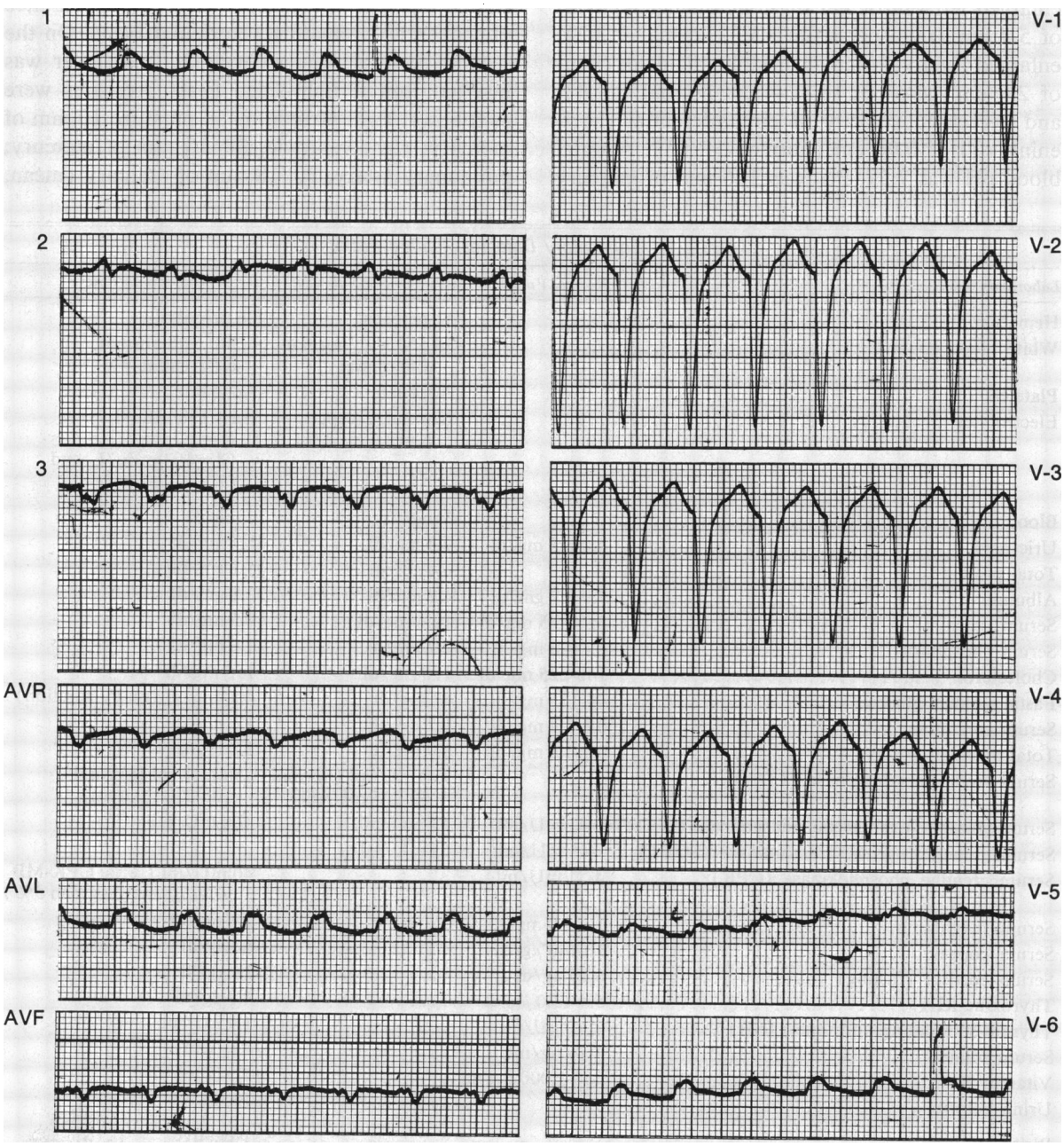


**Figure 1.**—Initial electrocardiogram showing a supraventricular tachycardia with aberrant conduction of the left bundle branch type (versus ventricular tachycardia) at 130 beats per minute.

intravenous hyperalimentation with Freamine II (McGaw Laboratories, Inc). and Intralipid (Cutter Laboratories, Inc.) totaling 1,300 calories per day. Also, potassium phosphate and one unit of plasma were given intravenously. By the seventh hospital day, the blood pressure did not exceed 70/50 mm of mercury by cuff pressures. The ECG (Figure 4) continued to show low voltages, and new ST-T wave changes and diffuse T wave inversions appeared. Digitalis was administered over the next few days. The blood pressure gradually increased, and by the ninth hospital day the urine output was normal without the use of diuretics.

On the 11th hospital day, three transvenous endomyocardial biopsy specimens were obtained from the right ventricle by previously described techniques.[6] Two of the specimens were adequate for study and were reviewed by the Department of Pathology at Stanford University Hospital. Light microscopy (Figure 5) showed degenerating and vacuolated myocytes, increased areas of fibrosis, compensatory myocyte hypertrophy and focal areas of myocyte necrosis with adjacent mononuclear cell infiltration. These changes were consistent with a nonspecific myocarditis.

On the 13th day, while the patient was on ECG telemetry, an asymptomatic nine-beat episode of ventricular tachycardia at 140 beats per minute was recorded. She was given an oral loading dose of diphenylhydantoin 900 mg, followed by 300 mg per day. Continuous monitoring showed that no further ventricular irritability occurred for the remainder of the hospital stay. In the third week of her hospital stay, the patient resumed eating a 1,500-calorie high-protein diet and continued to improve. A repeat echocardiogram (Figure 6) showed a normal-sized left ventricle with normal wall motion. The discharge ECG showed continued low voltages in the standard leads with diffuse T wave inversions and normal QT interval. After three weeks in hospital, she was discharged on a

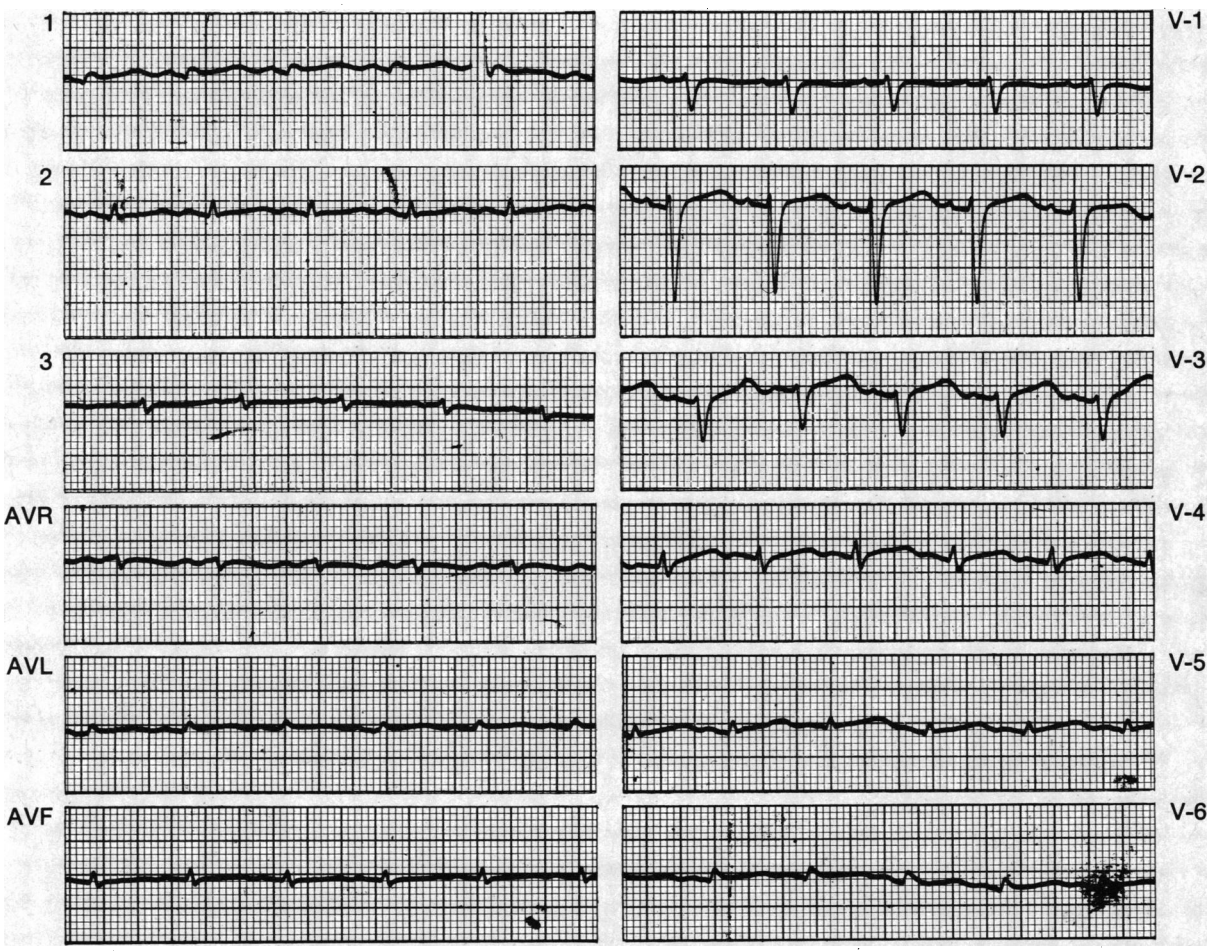


**Figure 2.—Two hours later electrocardiogram shows sinus tachycardia 100 beats per minute.**

regimen of digoxin, diphenylhydantoin, ferrous sulfate (for a phlebotomy-induced anemia) and multivitamins with copper. Four months after discharge, she had returned to normal activities and was maintaining her weight at 65 kg (143 pounds) on a 1,500-calorie diet. Follow-up studies included a nuclear angiogram three months after discharge which showed mild generalized hypokinesis with a calculated ejection fraction of 0.55 (normal 0.57 to 0.74).

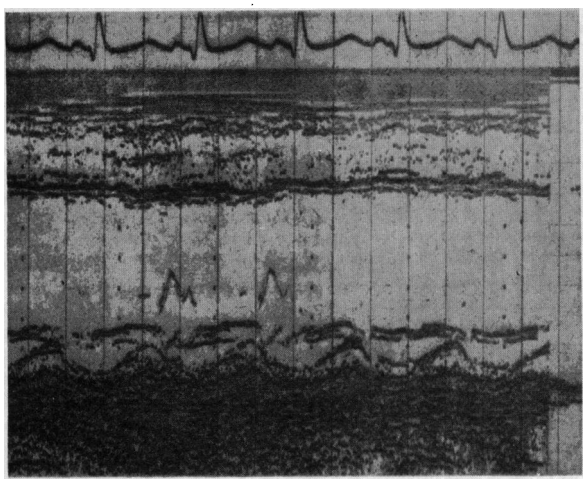

**Figure 3.**—Echocardiogram with transducer beam directed through the left ventricular cavity showing decreased septal motion and thickness with an enlarged ventricular diastolic diameter.

## Discussion

Starvation in nonobese patients is associated with hemodynamic alterations and pathological changes in the heart. The arterial blood pressure, venous pressure and pulse pressure tend to diminish while extracellular volume increases relative to body weight. Keys[7] reported that autopsy showed a reduction in heart size commensurate with the total loss of body weight. Microscopically, there tends to be a decrease in size of the heart muscle fibers followed by evidence of muscle degeneration. Reports of patients with

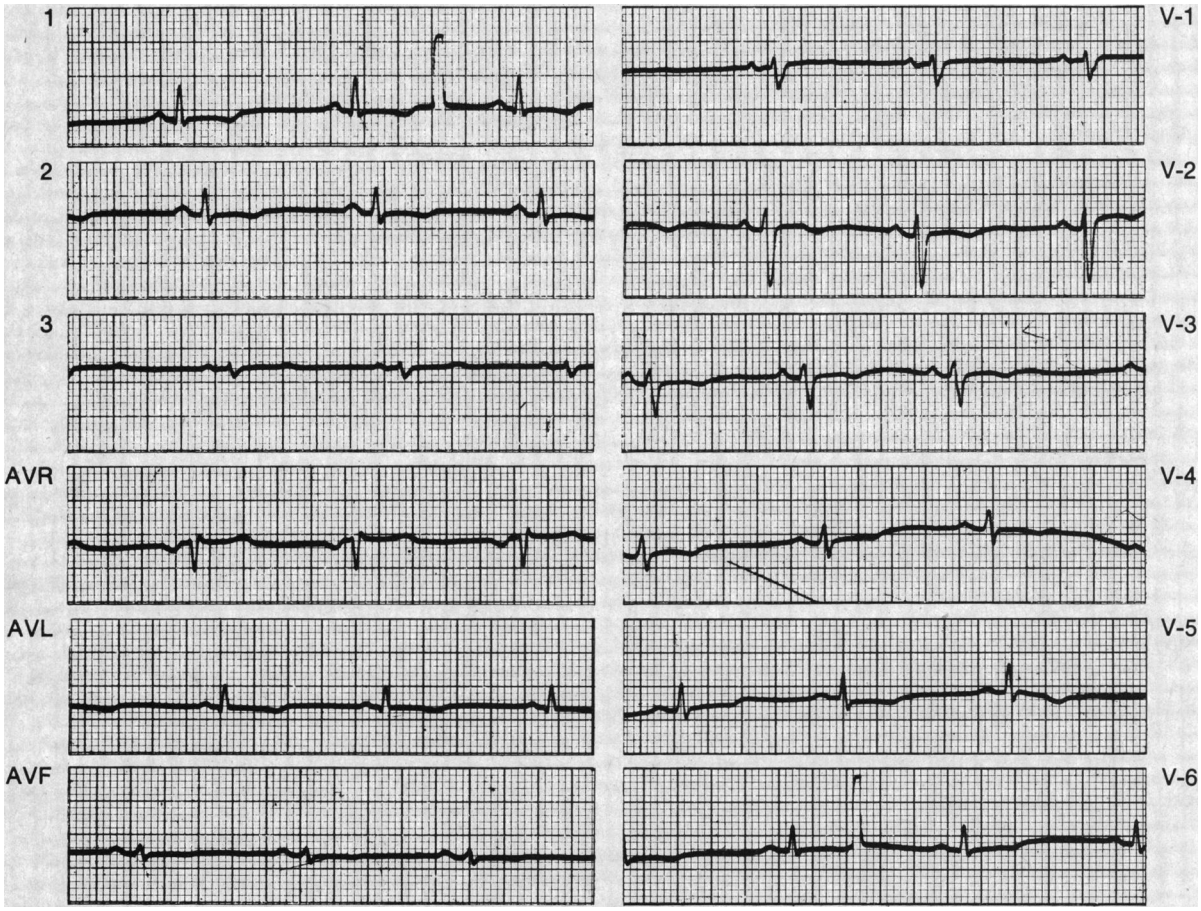


**Figure 4.**—On the seventh day electrocardiogram shows low voltages and new ST-T wave changes and diffuse T wave inversions.

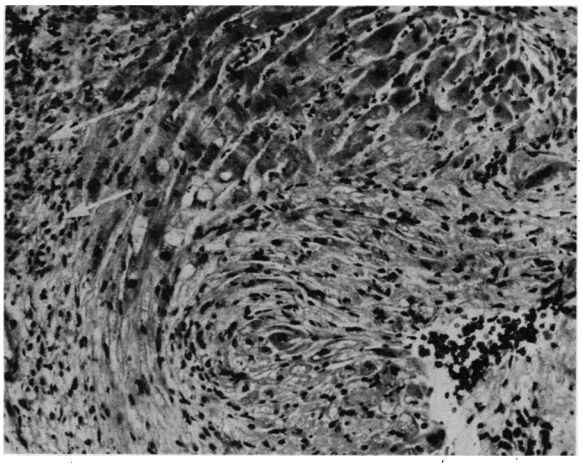

**Figure 5.**—Right ventricle, endomyocardial biopsy. The arrows show fibrosis with mononuclear cell infiltrates. Adjacent area shows myocyte necrosis and degeneration with compensatory hypertrophy and vacuolation of myocardial fibers. Magnification reduced from ×190.

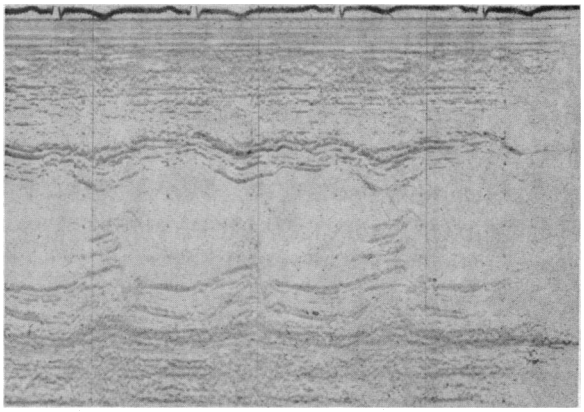

**Figure 6.**—Echocardiogram with transducer beam directed through the left ventricular cavity at the end of the third week. The septal motion and left ventricular diastolic diameter are normal.

kwashiorkor or marasmus[8-10] have emphasized that the majority have ECG changes often associated with extensive nonspecific myocardial changes discovered by autopsy. Echocardiograms in patients with several forms of wasting diseases have revealed a decreased left ventricular mass (although proportionally less decrease than that of body mass), but normal ejection fraction and velocity of circumferential shortening ($V_{cf}$).[11]

In previously healthy obese patients, prolonged total starvation has been reportedly well tolerated without complications for periods up to 249 days.[1] However, sudden death as a consequence of total caloric restriction of relatively short duration has been reported in patients with preexisting evidence of heart disease.[12] There are two case reports of cardiovascular complications associated with prolonged starvation in otherwise healthy individuals on metabolic wards. Garnett and co-workers[2] reported the case of a 20-year-old woman who died after 30 weeks of "total starvation" (actually, amino acid supplements were used for at least eight weeks). She died of ventricular fibrillation one week after low-caloric refeeding. The electrocardiogram showed QT interval prolongation in the absence of electrolyte imbalance, or use of antiarrhythmic or diuretic drugs. Postmortem examination of the heart showed a paucity and disruption of cardiac myofibrils only on electron microscopy. Sandhofer and associates[3] reported on a 37-year-old woman who had been on a total fast with vitamin and mineral supplements. Following excessive physical activity, she collapsed due to fatigue and hypotension. The ECG showed sinus tachycardia, low voltages and QT interval prolongation. She was gradually refed, and she made an uneventful recovery. The electrocardiographic abnormalities, however, persisted for 11 weeks.

Recently, a number of sudden cardiac deaths have been reported in otherwise healthy obese people on liquid protein-modified fasts for periods of two to eight months.[4,5] Some had resumed normal diets at the time of death. The ECG's frequently showed prolonged QT intervals and low voltages. Serum potassium levels ranged from 2.1 to 4.1 mEq per liter. Serum calcium, phosphorus and magnesium values were in the low normal range. Autopsy findings in 14 such cases showed evidence of myocarditis in seven and degeneration of myocytes without inflammation in two; documented cause of death was ventricular fibrillation. Anecdotal reports[13] have noted the successful treatment of these arrhythmias with diphenylhydantoin following failure of response to more conventional antiarrhythmic medications.

The pathological findings in our case, obtained from an endomyocardial biopsy specimen from the right ventricle, showed a myocarditis similar to those reported among some users of the liquid protein-modified diets. However, our patient did not receive protein supplements and had fasted four months before admission to hospital. Her weight at time of admission (62 kg or 136 pounds) was consistent with an expected weight loss in total starvation of 1.75 kg per week, but was 12 kg more than her ideal weight of 50 kg (110 pounds). The hemodynamic, echocardiographic

and nuclear angiographic studies suggested biventricular failure due to a congestive cardiomyopathy as evidenced by a wide AV difference, high PAW pressure and left ventricular dilatation and impaired contractility. The oliguria and metabolic acidosis might have been secondary to salt and water retention that occurs with carbohydrate refeeding after starvation or the low cardiac output state (or both). The ECG abnormalities were consistent with a diffuse myocarditis which was substantiated by the endomyocardial biopsy findings. The transient appearance of supraventricular tachycardia with left bundle branch block (or ventricular tachycardia) may have reflected inflammatory involvement of the conduction system, or it may have been secondary to metabolic changes in cardiac conducting mechanisms.

Although associated with starvation, the cause of our patient's heart disease remains uncertain. The elevated liver enzymes are not usually characteristic of prolonged starvation[14] and may have been due to hepatic congestion. There may have been a coincident viral myocarditis; or there may have been a nonspecific inflammatory myocarditis in response to a chemical that was present in, or absent from, this patient's diet. For example, mineral supplements were used in this case and in the cases (resulting in cardiac deaths) reported by Garnett[2] and Sandhofer.[3] However, there were no additional findings of a systemic inflammatory disease, acute and convalescent viral titers were not obtained, and the use of mineral supplements may be only coincidental.

Total body potassium loss is a frequent accompaniment of total fasting.[1-3] Runcie and Thomson[14] reported that 2 of 18 patients after prolonged fasting experienced a "shock-like" state associated with increased levels of sodium and potassium in the urine, which were reversed by refeeding or with potassium chloride. Despite supplemental potassium chloride, several patients spontaneously (and one patient after a carbohydrate load for a glucose tolerance test) developed pronounced hypokalemia as low as 2.4 mEq per liter. In addition, hypokalemic myocardial lesions that have been produced in rats by a potassium-deficient diet[15] resemble the nonspecific myocarditis reported in this case and in some users of liquid protein-modified diets. In man, however, these myocardial lesions are usually reflected in specific hypokalemic electrocardiographic patterns which were absent in this case.

Coronary artery disease in a patient of this age and sex would be unlikely, more so in the absence of chest pain, typical ECG changes, or elevation of the creatine phosphokinase (CPK) myocardial isoenzyme.[16] Hypophosphatemia reportedly retards myocardial stroke work;[17] but there is usually a rapid improvement following phosphate repletion, which did not occur in our patient. Finally, copper deficiency has been associated with myocardial atrophy in animals.[18] In our patient serum copper level was slightly decreased and she received plasma while she was not eating because we hoped to replenish the copper in her serum.

We conclude that the heart may not be spared during prolonged fasting. Serious cardiac damage and death may ensue whether one uses a protein-modified fast or prolonged starvation alone. Close medical supervision on an outpatient basis or observation on a metabolic ward may allow early detection and correction of metabolic abnormalities and myocardial dysfunction that may be precipitated by increased physicial activities or with refeeding. However, even if the patient has continuous ECG monitoring, there may be little protection against the unpredictable onset of serious ventricular arrhythmias and sudden death. Finally, the prognosis for patients who develop endomyocardial biopsy evidence of myocyte destruction during prolonged fasting is unknown.

## Summary

Recently a number of cardiac deaths have been associated with fasting modified by liquid protein supplementation. We report a case of a 26-year-old woman who developed biventricular congestive heart failure after having fasted for four months without protein supplementation. Examination of an endomyocardial biopsy specimen showed a nonspecific myocarditis similar to the pathological findings in users of the liquid protein-modified diets. We concluded that serious cardiac damage and death may occur in patients who undertake a prolonged fast with or without liquid protein supplementation.

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# Scurvy Resulting From a Self-Imposed Diet

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SCURVY IS A RARE disorder usually occurring in older persons who live alone[1,2] or in infants and children secondary to parental ignorance or neglect.[3,4] Occasionally, scurvy can occur in young or middle-aged adults secondary to psychoneurosis and poor eating habits,[5] fad diets,[6] and restricted diets.[7]

We report a case of scurvy in a 43-year-old woman on a self-imposed diet. Early skin and nail changes are presented along with histopathological findings. This patient was initially diagnosed as having allergic vasculitis.

## Report of a Case

A 43-year-old woman came to the outpatient clinic of the University of California, San Diego, for evaluation of her skin lesions. She had been followed during the previous three years by private physicians, including a psychiatrist, for complaints of fatigue, weakness, depression, arthralgias and intermittent abdominal pains. No abnormalities had been found and she was felt to have a hypochondriacal neurosis with delusions. However, in September 1977 she noted the development of "red bumps" over the skin of her legs, thighs and arms. Initial evaluation revealed a hemorrhagic skin eruption with splinter hemorrhages of her fingernails and a 6.8-kg weight loss during the previous three months. Blood pressure was 118/70 mm of mercury sitting, and pulse was 96 beats per minute. A diagnosis of allergic vasculitis and possibly a subacute bacterial endocarditis was considered at that time. Results of laboratory tests, including complete blood count, analysis of urine, SMA-12, prothrombin time and partial thromboplastin time, were within normal limits. Venereal Disease Research Laboratories test and tests for rheumatoid factor, antinuclear antibody and cryoglobulins yielded negative results. Serum complement $C_3$, $C_4$ and $CH_{50}$ levels were normal. Blood, urine, throat and sputum cultures showed no growth.

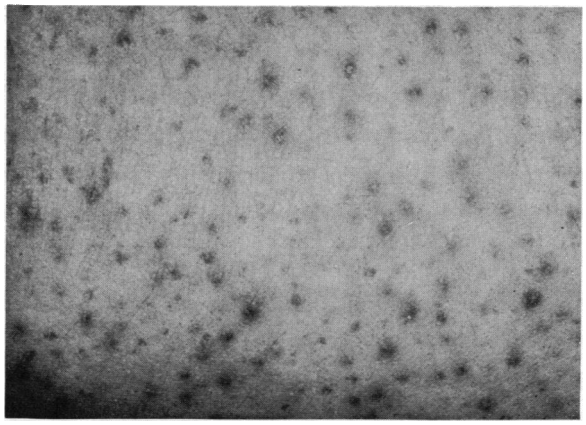

**Figure 1.—Hyperkeratotic follicular papules with hemorrhage over the anterior thigh. Coiled hairs are present in the follicular plugs.**

The patient was seen in consultation at the dermatology clinic. Hyperkeratotic and hemorrhagic papules were noted over both lower and upper

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Submitted August 22, 1978.

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