has been tried. Respiratory stimulation is usually but
part of a general stimulation of the central nervous
system (CNS), and the dose needed to produce a sig-
ificant increase in minute ventilation has been very
close to the dose that causes convulsions.

Our patient showed transient improvement with in-
travenous ethamivan therapy, but this increase in minute
ventilation could not be maintained with oral medica-
tion.

While MPD is less effective as a respiratory stimulant
than some other analeptics, previous studies have been
with parenteral or aerosolized modes of administra-
tion, and there are no reports of the use of MPD
orally for this purpose. It does have fewer neuromus-
cular side-effects, and may therefore lend itself bet-
ter to long range therapy. Like all centrally acting
synthetic amines, at least when given subcutaneously,
MPD produced an increase in respiratory rate. Trial
of oral MPD in our patient was on an empiric basis,
as she was deteriorating, and we had had little suc-
cess with other modes of therapy. With institution of
MPD, she showed a prompt and continued improve-
ment in minute ventilation and marked decrease in som-
nolence and lethargy. This improvement has been main-
tained for nine months. We report this case so that others
may try this form of therapy.

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Idiopathic Isolated Right
Ventricular Cardiolithiasis*

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A rare case of isolated idiopathic right ventricular
endocardial calcification with outflow tract obstruction,
organized pulmonary emboli, and subsequent right heart
failure is presented. Diagnostic features, possible etiolo-
gies, investigation and treatment are outlined. This case
is believed to be the first of its kind reported in North
America.

In this era of increasingly sophisticated radiologic
equipment and trained personnel, cardiac calcification
is becoming more commonly recognized. It is esti-
ated to be present in excess of 10 percent of patients
with either primary or secondary clinical heart disease.
It should be recognized, however, that the frequency of
this phenomenon varies as to the etiology, cardiac struc-
tures involved, limitations of equipment utilized and,
last but not least, the awareness and persistence of the
radiologist. Holmes has outlined a method of diligent
search for cardiac calcification utilizing modern fluoros-
copic techniques that can reveal minute isolated calcifi-
cations as small as 1.5 mm. Early and accurate diagnosis
of cardiac calcification can be exceptionally helpful in
the management of heart disease.

In decreasing order of frequency, calcium may be
found in valves, pericardium, coronary arteries, ven-
tricles, ventricular aneurysms and atria. Isolated endo-
cardial ventricular calcifications secondary to endomy-
cardial fibrosis, while found in 5.9 percent of cases in
Equatorial Africa, are exceptionally rare in North
America. This report concerns a case of isolated endo-
cardial right ventricular calcification. Possible etiologies
and early definitive treatment of this condition prior to
potentially irreversible right-sided heart failure are dis-
cussed.

CASE REPORT

The patient was an obese, postmenopausal, para O, gravida

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O, 47-year-old Caucasian, with Class 3E cardiac disease (New York Heart Association), and a known heart murmur for nine years. She had experienced a two-year crescendo course of increasing fatigue, weakness, dyspnea, precordial palpitations, ankle edema, ascites, "two-pillow" orthopnea, anorexia, intermittent jaundice, nausea and central cyanosis. There was no history of phlebitis, intravenous drug abuse, flushing attacks, diarrhea, angina pectoris, hypertension, renal calculi, arthralgias, connective tissue disorders or endocarditis. She did, however, recall frequent bouts of typical pleuritic chest pain, and had a remote history of hepatitis.

Physical examination following admission to the hospital revealed a lethargic, cyanotic, orthopneic woman with deep scleral icterus. Jugular venous pulsations of 8 cm were noted above the sternal angle (30° supine head-up position), with absent A-waves, predominant V-waves, and a negative Kussmaul's sign. Tachypnea of 36/min with both central and peripheral cyanosis was apparent. No hypertrophic osteoarthropathy was present. High, poorly mobile diaphragms with bilateral posterior basal post-tussive rales and a few scattered sonorous rhonchi were noted. The blood pressure was 120/60 mm Hg with no significant paradox. The cardiac rate was irregularly irregular at 122/min. The cardiac apex was not palpable. There was a marked left parasternal heave with a possible systolic thrill and a definite pulmonic closure tap palpable. A harsh grade 4/6 ejection systolic left parasternal (third interspace) nonradiating murmur accentuated with inspiration and a loud P2 with wide, almost fixed splitting were audible. A prominent right ventricular gallop was also heard, but no ejection click or diastolic blow was noted. All peripheral pulses were decreased with no pathologic paradox. There was dependent edema up to the sacral area and ascites was easily demonstrated.

The patient's hospital course consisted mainly of atrial tachy-brady dys律rhythmias controlled primarily with digi脦alis therapy. Temporary endocardial pacing was necessary on one occasion, possibly secondary to digitalis toxicity (Fig 1). Severe right-sided heart failure with moderate left-sided failure almost refractory to orthodox methods of management and severe systemic hypoxemia with borderline hepatic decompensation were prominent features of her hospital stay.

In addition to her dys律rhythmias, electrocardiograms showed right bundle branch block, right ventricular hypertrophy and strain, marked right axis deviation (+120°), low voltage and digitalis effect. A chest x-ray film revealed cardiomegaly with predominant right ventricular enlargement and outflow tract calcification (Fig 1), plus a few scattered, small, calcified right pulmonary nodules.

Pertinent laboratory abnormalities included the following values: erythrocyte sedimentation rate, 55 mm/hr; serum bilirubin (direct), 3.5-5.0 mg/100 ml, (indirect) 1.4-3.5 mg/100 ml; ammonia, 90 μg; alkaline phosphatase, 140 KA units; serum glutamic pyruvic transaminase 68 units; prothrombin time, 58 percent; and results of serologic test for syphilis (VDRL), weakly reactive. The urine showed 1+ protein, 3+ bilirubin, 1+ urobilogen and 4+ bacilli. Complete blood count and serum electrolytes, phosphorus, urea, glucose (fasting), lactic dehydrogenase, creatine phosphokinase, serum glutamic oxaloacetic transaminase levels, iron and iron binding capacity were normal. Lupus erythematosus cell preparation results were negative and six blood cultures yielded no organisms.

**Necropsy Findings**

Death was sudden after four days of hospitalization.

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the right ventricular outflow tract by about 85 percent. There was calcific fibrosis with some contracture of a papillary muscle limiting coaptation of the anterior tricuspid leaflet. The chordae tendineae appeared normal. The tricuspid, pulmonary, mitral and aortic valves were normal in appearance and circumference. There were no other abnormalities of the endocardium or myocardium. The coronary arteries showed little atheromatous change. The right coronary artery was large and dominant, supplying most of the right ventricle and giving rise to the posterior descending branch to the apex of the left ventricle.

Microscopic examination of the heart (right ventricle) revealed marked subendothelial fibrosis with extensive hyalinization and evidence of calcification. Broken masses of elastic fibers were present in a few areas, but in general elastosis was minimal to absent. Small scattered groups of subendothelial lymphocytes were present. Fibrosis extended slightly into the subjacent myocardium. Virtually acellular, hyalinized material with evidence of extensive calcification was attached to the abnormal right ventricular endocardium. Sections from the left ventricle showed minimal pathologic changes.

The lungs showed dense diffuse pleural adhesions bilaterally; no free pleural fluid was present. Marked dependent pulmonary congestion was noted, but no areas of infarction or consolidation could be demonstrated. The right main pulmonary artery contained a smoothly lobulated, globoid, calcific semi-sessile mass 1.3 cm in diameter, firmly attached to the arterial wall (Fig 4, 5). This lesion produced about 50 percent occlusion of the lumen. A few minute calcific masses were also noted within the right distal pulmonary vascular tree. No other evidence of thromboembolic disease was apparent. A few small lipoid intimal plaques were present just distal to the calcific nodule in the right main pulmonary artery. The left main pulmonary artery appeared normal.

Microscopic examination of the lungs showed generalized thickening of the alveolar walls with hemosiderin-laden macrophages free in alveolar spaces. Many small and medium-sized muscular pulmonary arteries showed moderate to marked medial hypertrophy with conse-

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**Figure 3.** Postmortem radiograph of heart showing right ventricular endocardial calcification at arrow.

**Figure 4.** End-on view of right main pulmonary artery showing yellow concretions at arrow.

**Figure 5.** Postmortem radiograph of right lung, with central right main pulmonary artery calcific lesion at arrow. Some smaller lesions may be seen in periphery.
Quent luminal narrowing; many others showed evidence of old thromboemboli with organization and recanalization. No fibrinoid necrosis was evident. The larger elastic arteries were normal except for small foci of intimal atheromata. The pulmonary arterioles were inconspicuous. Sections of the decalcified lesion in the pulmonary artery showed a hypocellular, fibrous stroma with minimal hyalinization. The underlying intima appeared normal.

The liver, which weighed 2,200 gm, and the spleen showed acute and chronic passive congestion. There were no biliary calculi. The kidneys and adrenals were acutely congested. The parathyroid glands were not obtained. No abnormal calcification was found outside of the right pulmonary arterial tree and right ventricle. Microscopic examination confirmed the gross observations, and no other pertinent pathologic changes were seen.

**Discussion**

Predominant right ventricular failure can be associated with various congenital and acquired lesions. If a complete history, physical examination, routine urine and blood analyses have failed to show the etiology, tests to exclude systemic diseases, including those which may produce primary or secondary cardiac calcification, must be performed. Also indicated is a radiologic examination by an experienced radiologist using image intensification fluoroscopy with "coning down" techniques in various body attitudes. When a radiologic examination reveals calcification in the heart, a determination should be made as to its significance, such as location and extent, by early cardiac catheterization with appropriate hemodynamic studies, dye curves and selective angiography.

Metastatic calcification as found in the primary or secondary hypercalcemic states usually results in calcium deposition in the normal tissues of such organs as lungs, stomach, kidneys, heart, and blood vessels. Dystrophic calcification, being far more common and generally associated with normocalcemic states, refers to the deposition of calcium in devitalized tissue (collagen) which is relatively quiescent and not undergoing rapid metabolism. This "scar tissue," producing little metabolic carbon dioxide, lactic acid and other organic acids, is therefore relatively alkaline. Consequently, calcium salts, which are less soluble in an alkaline medium, are readily precipitated.

In this case no evidence of primary or secondary hypercalcemic states was found either on ante- or post-mortem examination. The laboratory data on serum calcium levels were unavailable, but the serum phosphorus value was normal. Therefore, a diagnosis of dystrophic as opposed to metastatic calcification is probable. The only other organ showing calcification was the right lung. This calcium deposit was completely intra-arterial and was probably embolic from the parent right ventricular lesion, which we feel was the primary cause for the right ventricular decompensation. The widespread pulmonary vascular changes (presumably related to repeated microemboli from the right ventricular mass) and the right main pulmonary artery lesion may have contributed to the right-sided heart failure. The elevated alkaline phosphatase levels and other abnormal liver function tests are considered to reflect the prolonged and intense hepatic congestion and cellular hypoxia. The etiology of the weakly reactive venereal disease research laboratory test was not determined, but there was no supportive evidence of active or inactive syphilis or connective tissue disorder.

We are left, therefore, with a case of primary isolated idiopathic endocardial right ventricular outflow tract calcification with obstruction and subsequent congestive cardiac failure.

Treatment, once a diagnosis is secure as to anatomy, is variable, since differentiation must be made between metastatic and dystrophic calcification. Calcium deposits secondary to hypercalcemic states may respond favorably to treatment of the primary disease process (eg, metastatic carcinoma, hyperparathyroidism, hyperparathyroidism-D, renal insufficiency, sarcoidosis, etc) with subsequent lowering of the serum calcium. The treatment of dystrophic calcification is that of arresting or slowing the degenerative disease process, with early surgical intervention if significant hemodynamic obstruction is demonstrated.

We believe that the incidence of isolated right-sided outflow tract calcification will increase in the next five to 15 years as a remote complication of healed bacterial endocarditis secondary to intravenous drug abuse. This diagnosis would be more readily attained if considered in the early stage of right ventricle overload, and a more concerted effort made at fluoroscopic examination. It is also important that early definitive treatment be instituted prior to obstruction and subsequent right ventricular failure with its appreciably increased morbidity and mortality.

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