Long-term Outcome of Pediatric Sarcoidosis with Emphasis on Pulmonary Status*

Roxanne Marcille, M.D.; Michael McCarthy, M.D.; John W. Barton, M.D.; David F. Merten, M.D.;† and Alexander Spock, M.D.

Sixty-one pediatric and adolescent patients (age ≤16 years) with sarcoidosis proved by biopsy specimen were identified during the period 1957 to 1976; 19 patients with elapsed time from diagnosis of 8 to 35 years (mean, 21 years) were reexamined in 1985. Age at onset of disease ranged from 4 to 16 years (mean, 12.5 years). Sex distribution was equal; 68 percent of individuals were black. At follow-up, clinical evaluation, chest roentgenograms, pulmonary function tests, electrocardiograms (ECGs), echocardiograms (ECHO), and angiotensin-converting enzyme (ACE) activity were performed on each subject. In addition, complete blood cell counts, erythrocyte sedimentation rates, serum calcium, immunoglobulin levels, B- and T-cell enumerations, and intradermal skin tests for delayed hypersensitivity were also obtained. Although all initial pediatric chest roentgenograms were abnormal, at follow-up only 37 percent were abnormal. Pulmonary function test results were available for ten children, and 90 percent were decreased. In 1985, 65 percent of the adults had abnormal lung function; furthermore, eight patients had reduced diffusing capacities, one had hypoxemia, and two had elevated ACE activity. Specific abnormalities were noted on two ECGs and 12 ECHOs. One individual had an elevated sedimentation rate, while another had an increased serum calcium level. Six patients had elevated IgA values, two had elevated IgM values, and two had depressed IgG values; IgG values were normal in all subjects. B- and T-cell percentages were unremarkable in all patients tested. Four individuals were anergic to skin test antigens. Long-term pulmonary morbidity was observed in four patients; in addition, one of these and four others suffered nonpulmonary sequelae. These results are in agreement with those of other investigators, but insufficient data still exist on the long-term effects of sarcoidosis on the pediatric host.

(Chest 1992; 102:1444-49)

ACE = angiotensin-converting enzyme; DOE = dyspnea on exertion; ECHO = echocardiogram; FEV, % = ratio of FEV, to FVC; LNH = left ventricular hypertrophy; LVEDD = left ventricular end-diastolic dimension; RAD = right axis deviation; RVEDD = right ventricular end-diastolic dimension; SOB = shortness of breath

Sarcoidosis with onset in childhood is less common than onset in the third and fourth decades of life. In 1985, we were able to study adult patients an average of 21 years after pediatric onset of disease. To our knowledge, these cases represent the longest follow-up series of pediatric sarcoidosis to date.

Materials and Methods

Sixty-one patients with childhood- or adolescent-onset sarcoidosis (age 16 years or younger) with disease proved by biopsy specimen were identified at Duke University Medical Center, Durham, NC, from 1957 to 1976. These individuals were selected as potential study subjects for evaluation of the long-term effects of pediatric sarcoidosis on their general health and well-being, with particular emphasis on pulmonary status.

Subjects were located through chart review, family members, local and referring physicians, telephone directories, marriage and driver's license search, and cross reference of names with the Society for the Blind. All individuals were invited to return to Duke in 1985 for a comprehensive medical evaluation. Of 20 patients who responded, 19 completed the evaluation process. Five deaths were noted from the original 61 sarcoid cases identified:

*From the Division of Pediatric Pulmonology, Duke University Medical Center, Durham, NC.
†Presented at the University of North Carolina at Chapel Hill. Manuscript received October 25, 1991; revision accepted April 8. Reprint requests: Dr. Marcille, Pulmonary Pediatrics, Duke University Medical School, Durham, NC 27710

The sex distribution of recruited subjects was essentially equal with ten male subjects and nine female subjects. Blacks outnumbered whites at a ratio of 2:2:1. Age on presentation in childhood ranged from 4 to 16 years with a mean age at diagnosis of 12.5 years. At reexamination, patients were 14 to 49 years old with a mean elapsed time from diagnosis of 21 years.

In addition to the pertinent patient history, a general health questionnaire was administered to each individual. Thereafter, each subject underwent physical examination, chest roentgenograms, pulmonary function testing (PFT), electrocardiogram (ECG), echocardiogram (ECHO), and various laboratory studies, including complete blood cell count, erythrocyte sedimentation rate, serum calcium, urinalysis, immunoglobulin levels (IgG, IgA, IgM), enumeration of T and B cells, angiotensin-converting enzyme (ACE) activity, and skin tests for delayed hypersensitivity (monilia 1:1,000 and intermediate strength PPD).

All roentgenograms, including initial and follow-up roentgenograms, were reviewed by a pediatric radiologist. Results were classified as normal, adenopathy alone (hilar, paratracheal, or both), parenchymal disease alone, or a combination of adenopathy and parenchymal disease. Staging of roentgenograms was in accordance with guidelines established by international convention. Complete pulmonary function tests included spirometry (Collins survey spirometer), lung volumes by helium dilution (Collins modular lung analyzer) and body plethysmography (Collins variable pressure body box), and diffusing capacity for carbon monoxide (Collins modular lung analyzer). Arterial pH and blood gas values were
determined by a pH/blood gas analyzer (Instrumentation Laboratory System 1301).

Predicted spirometric values for children were based on measurements established by Weng and Levison, whereas adult values were derived from Morris et al. Based on chart review, 10 of 19 patients had had PFT at diagnosis; as these early data were obtained on variable equipment, only general trends in lung function over time will be discussed. PFTs were classified as normal, restrictive, obstructive, or a combination of restrictive and obstructive. Criteria for restriction were based on a TLC of less than 80 percent predicted with a greater than 80 percent predicted FEV1, FEV/FVC, and/or FEF25-75%. Obstruction was considered to be present if TLC was normal, and FEV1, FEV/FVC, and/or FEF25-75% were less than 80 percent predicted.

Although diffusing capacities were performed on all adults in 1985, similar data were available for only two individuals as children and have not been included. A Deco of less than 80 percent predicted of the norms established by Ogilvie et al was considered a reduced value. Hypoxemia was defined as a PaO2 of less than 65 mm Hg on a room air arterial blood gas.

ACE activity, utilizing the hippuryl-L-histidine-L-leucine substrate method, was determined by a reference laboratory. ACE activity greater than 2 SDs from the reference laboratory mean (normal, 22.6±6 U/ml; range, 12 to 35 U/ml) was indicative of increased enzyme activity.

Twelve-lead ECGs and 2-D and M-mode ECHOIs were performed in the Duke University Hospital Cardiac Diagnostic Unit; all interpretations were reviewed by both adult and pediatric cardiologists.

The Duke University Pediatric Immunology Laboratory was responsible for the determination of immunoglobulin levels and B- and T-cell enumerations; lymphocyte percentages were derived from methods established by Schiff et al. All other laboratory samples were processed by the Duke University Clinical Pediatric Laboratory, and results were compared with the published norms for this clinical service.

RESULTS

Individual patient data are summarized in Table 1.

Table 1—Summary of Patient Data*

<table>
<thead>
<tr>
<th>Case/Sex/Race</th>
<th>Age at Presentation, yr</th>
<th>Age in 1985, yr</th>
<th>Roentgenogram</th>
<th>PFT</th>
<th>Deco</th>
<th>PaO2</th>
<th>ACE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial 1985</td>
<td>Initial 1985</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/M/B</td>
<td>5</td>
<td>37 A</td>
<td>— R</td>
<td>89</td>
<td>91</td>
<td>17.9</td>
<td></td>
</tr>
<tr>
<td>2/F/W</td>
<td>15</td>
<td>36 A</td>
<td>N —</td>
<td>75</td>
<td>92</td>
<td>15.9</td>
<td></td>
</tr>
<tr>
<td>3/M/B</td>
<td>14</td>
<td>38 A/PD</td>
<td>N R O</td>
<td>84</td>
<td>88</td>
<td>27.3</td>
<td></td>
</tr>
<tr>
<td>4/M/W</td>
<td>14</td>
<td>44 A/PD</td>
<td>ND</td>
<td>106</td>
<td>80</td>
<td>31.9</td>
<td></td>
</tr>
<tr>
<td>5/F/B</td>
<td>16</td>
<td>34 A/PD</td>
<td>PD R O</td>
<td>72</td>
<td>86</td>
<td>19.7</td>
<td></td>
</tr>
<tr>
<td>6/F/B</td>
<td>12</td>
<td>35 A/PD</td>
<td>ND</td>
<td>100</td>
<td>86</td>
<td>23.3</td>
<td></td>
</tr>
<tr>
<td>7/M/B</td>
<td>12</td>
<td>36 A/PD</td>
<td>ND</td>
<td>98</td>
<td>89</td>
<td>37.6</td>
<td></td>
</tr>
<tr>
<td>8/F/B</td>
<td>14</td>
<td>49 A/PD</td>
<td>ND</td>
<td>111</td>
<td>75</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>9/F/B</td>
<td>4</td>
<td>14 PD</td>
<td>PD R O</td>
<td>49</td>
<td>96</td>
<td>34.7</td>
<td></td>
</tr>
<tr>
<td>10/M/B</td>
<td>13</td>
<td>24 A</td>
<td>— R</td>
<td>61</td>
<td>81</td>
<td>46.6</td>
<td></td>
</tr>
<tr>
<td>11/M/B</td>
<td>12</td>
<td>20 A/PD</td>
<td>A/PD R O</td>
<td>66</td>
<td>68</td>
<td>64.5</td>
<td></td>
</tr>
<tr>
<td>12/F/W</td>
<td>13</td>
<td>39 A</td>
<td>— N</td>
<td>115</td>
<td>71</td>
<td>35.4</td>
<td></td>
</tr>
<tr>
<td>13/M/B</td>
<td>10</td>
<td>34 A</td>
<td>— O</td>
<td>93</td>
<td>101</td>
<td>23.4</td>
<td></td>
</tr>
<tr>
<td>14/F/B</td>
<td>15</td>
<td>36 A/PD</td>
<td>ND</td>
<td>98</td>
<td>70</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>15/F/B</td>
<td>15</td>
<td>35 A/PD</td>
<td>A/PD N R O</td>
<td>57</td>
<td>92</td>
<td>32.0</td>
<td></td>
</tr>
<tr>
<td>16/M/W</td>
<td>12</td>
<td>29 A</td>
<td>O N</td>
<td>105</td>
<td>91</td>
<td>34.2</td>
<td></td>
</tr>
<tr>
<td>17/M/W</td>
<td>15</td>
<td>30 A</td>
<td>— N</td>
<td>67</td>
<td>105</td>
<td>16.9</td>
<td></td>
</tr>
<tr>
<td>18/M/W</td>
<td>15</td>
<td>28 A/PD</td>
<td>N O O</td>
<td>83</td>
<td>70</td>
<td>33.2</td>
<td></td>
</tr>
<tr>
<td>19/F/B</td>
<td>13</td>
<td>41 A/PD</td>
<td>N R R O</td>
<td>44</td>
<td>54</td>
<td>24.6</td>
<td></td>
</tr>
</tbody>
</table>

* M = male; F = female; B = black; W = white; A = adenopathy alone; PD = parenchymal disease alone; A/PD = adenopathy plus parenchymal disease; PFT = pulmonary function test; ACE = angiotensin-converting enzyme; N = normal; R = restrictive; O = obstructive; R+O = restrictive plus obstructive.

Chest roentgenograms were abnormal in all children at presentation. A combination of adenopathy and parenchymal disease was observed in 53 percent of patients, adenopathy alone in 42 percent, and isolated parenchymal disease in 5 percent. At follow-up, 68 percent of the adults had resolution of all initial roentgenographic findings (Fig 1). Of those individuals with parenchymal involvement at reexamination, 83 percent were noted to have had parenchymal disease on their pediatric roentgenograms. Pulmonary func-
tion data from childhood were available for only ten subjects, and all but one had results that were indicative of reduced lung volumes and/or flows. Restrictive pulmonary function was observed in four patients, obstruction in three others, and a combination of restriction and obstruction in the remaining two children. Of these nine subjects, only two had normal pulmonary function test results as adults. Two-thirds of patients in 1985 had reduced lung functions, with obstruction to airflow more commonly observed than restriction. In general, roentgenographic parenchymal disease tended to be associated with abnormal pulmonary function, but the latter was as frequently associated with a normal chest roentgenogram as with an abnormal one.

Diffusing capacities for carbon monoxide were normal in 42 percent of subjects at follow-up. A Deco less than 80 percent predicted was noted in eight patients; four of the eight had roentgenographic evidence of parenchymal disease, and five had restrictive lung function. Only one subject was hypoxemic (PaO₂ less than 65 mm Hg on room air) by blood gas determination. No correlation was observed between isolated PaO₂ values and roentgenographic abnormalities or with PaO₂ and reduced pulmonary function or diffusing capacities. Elevations of ACE activity were documented in only two patients; one had parenchymal changes on chest roentgenograms, whereas both had lung function testing indicative of restriction.

A positive history of smoking was elicited in 11 of the 19 adults polled; three individuals, however, reported only minimal tobacco exposure (less than 2 years) and were thus classified as nonsmokers. Three-fourths of smokers had normal chest roentgenograms at follow up as did three of four nonsmokers. Half of the smokers had normal pulmonary function while the other half had reduced lung function; only one of nine nonsmokers had normal PFTs.

Specific abnormalities were observed in two ECGs: one patient had primary atrioventricular (AV) block, left ventricular hypertrophy (LVH), and nonspecific T-wave changes; the other had sinus bradycardia, right ventricular hypertrophy (RVH) with strain, right axis deviation (RAD), T-wave abnormalities in the precordial leads, and a history of cor pulmonale. Only five of 17 patients had normal ECHOs. Two others had concentric LVH, and three had right ventricular end-diastolic dimensions (RVEDD) at the upper limits of the normal range for adults. Of interest, seven subjects had RVEDDs that exceeded the norm with septal and posterior wall thicknesses that were either increased or at the upper limits of normal for this measurement. In addition, six of these patients had abnormal pulmonary artery (PA) Doppler's that were indicative of systolic blood flow turbulence.

Complete blood cell counts revealed the following values: mean hematocrit of 43 percent (range, 35 to 51 percent), mean hemoglobin of 14.3 g/dl (range, 11.6 to 16.2 mg/dl), and mean leukocyte count of 5,750/mm³ (range, 3,000 to 8,600/mm³); the average differential cell counts were 67 percent for neutrophils and 37 percent for lymphocytes. Only one patient had a mildly elevated sedimentation rate (30 mm/h). Serum calcium values ranged from 9.2 to 11.1 mg/dl with a mean of 9.8 mg/dl; again, only one individual had an elevated serum calcium level (11.1 mg/dl). All subjects had normal results of urinalyses.

Immunologic studies included IgG, IgA, and IgM levels; cellular immunocompetent B- and T-cell values; and skin tests for delayed hypersensitivity (monilia and intermediate-strength PPD). The mean IgG level was 1,240 mg/dl (range, 848 to 2,100 mg/dl), the mean IgA level was 572 mg/dl (range, 240 to 1,100 mg/dl), and the mean IgM was 74 mg/dl (range, 32 to 192 mg/dl). All IgG values fell within the established norms for age and race;¹⁴ the mean IgC for white subjects was 1,080 mg/dl and for blacks, 1,418 mg/dl. Six patients (32 percent) had elevated IgA values, two of whom had values of 1,000 mg/dl or greater. Two others had increased IgM levels while another two had depressed levels. Of the 11 immunocompetence profiles performed, all B- and T-cell percentages were normal except one individual with slightly low B-cell values.

Sixteen patients returned information on their intradermal skin testing; five subjects reported no response to either monilia or tuberculin antigens, and one of these five was still receiving daily steroids (20 mg). Two individuals had greater than 10 mm induration of their PPD at 48 h, while another three had 5-mm reactions. None of these patients had clinical evidence of tuberculosis.

Multiple attempts were made to obtain documentation of prior steroid therapy in these patients from their primary care physicians. As this information was not made readily available, we are able to comment on this issue solely based on each individual medical history and health questionnaire. Four subjects were treated with steroids for periods of six to 12 months at diagnosis, two had never received steroids, one had had intermittent therapy, one took steroids for 19 years, and two have been maintained on continuous therapy since diagnosis (18 and 20 years, respectively). Nine patients either could not recall steroid exposure or could not remember specific dosages or duration of treatment.

At follow-up, four individuals were considered to have chronic sarcoidosis, defined as disease of at least two years' duration.¹ One young woman had stable dyspnea on exertion (DOE), mild reactive airways disease responsive to aerosolized bronchodilators, and no history of steroid therapy. The remaining three
patients were receiving daily prednisone at dosages of 5 mg, 20 mg, and 25 mg, respectively. Steroids were necessary to alleviate symptoms of cough and/or DOE in two subjects, while the third had chronic iritis that remained quiescent on 5 mg of prednisone a day.

Eleven patients reported shortness of breath (SOB) and DOE at reexamination. Seven of these subjects had SOB and/or DOE purportedly due to obesity, cigarette smoking, heart disease, or a combination of these factors. Four others had similar respiratory complaints in the absence of any such predisposing conditions. Moderate to severe loss of lung function (TLC, FVC, and FEV₁ all less than 60 percent predicted) was observed in four patients; clinically, three of these individuals met the criteria for chronic sarcoidosis. Nonpulmonary sequelae were identified in five subjects and included legal blindness (three), persistent Bell's palsy (one), chronic back pain from bony vertebral involvement (one), and cor pulmonale (one).

**DISCUSSION**

Our series of patients is comparable to those of earlier reports in mean age at presentation, sex distribution, and, at least in the United States, an increased incidence in blacks.15-22 The mean elapsed time from diagnosis to reexamination in 1985 for these subjects was 21 years. Six earlier pediatric reports quote mean times to follow up of from 2 to 9 years (n = 8 to 51 patients); the University of North Carolina has observed some individuals for as long as 23 years, but their overall mean follow-up period was 4.7 years.15,16,18-21

The most common initial chest roentgenogram abnormality noted in these series was a combination of hilar and/or paratracheal adenopathy and parenchymal disease, followed by adenopathy alone (usually hilar); isolated parenchymal changes were uncommon. By international convention, these roentgenographic patterns correspond to stages II, I, and III disease.8 In adults, hilar adenopathy alone is the most frequently cited roentgenographic pattern on presentation, while isolated parenchymal abnormalities may be seen in up to 30 percent of patients.1,5,24,25 These age-related roentgenographic differences most likely arise from diagnosis of sarcoidosis through mass roentgenographic screening techniques of large cohorts of asymptomatic adults. In countries where routine chest roentgenograms of substantial numbers of school-age children have been performed, hilar adenopathy alone is also the most common roentgenographic pattern observed.17,26 The resolution rate of chest roentgenographic abnormalities over time (all stages combined) in our subjects was 70 percent; this concurs with data from prior reports in both children and adults.3,17,22,24,25

Few pediatric series have extensive data on PFT in sarcoidosis.15,30-22 Though small in number, our results support earlier observations that “restriction” is the most common acute disturbance in lung function observed in these patients. Unlike roentgenographic findings, however, normalization of pulmonary function over time did not necessarily occur, and obstruction to air flow was more common than restriction. Although sarcoid lung involvement classically results in a restrictive functional defect, several authors have documented abnormalities of pulmonary function not explained by reduced lung volumes alone.27-29 Indeed, increased airway hyperreactivity with methacholine challenge has been documented previously in individuals with sarcoidosis.30

Abnormal roentgenographic findings did not reliably predict abnormalities of pulmonary function and vice versa. Several subjects with normal chest roentgenograms were found to have decreased lung function, while others with abnormal roentgenograms had normal lung function. The noncorrelation of clinical data with disease activity in sarcoidosis is well accepted.1,2-3,38 Certain trends, however, reflecting extremes of disease were notable at follow-up: individuals with normal PFTs had normal chest roentgenograms, while those with isolated parenchymal disease had reduced lung function.

The determinations of diffusing capacity, arterial PO₂, and ACE activity were likewise not predictive of chest roentgenographic findings or disturbance of lung function except again in certain instances of extremes of disease. Those patients with the most reduced diffusing capacities were observed to have the lowest arterial oxygen values, while those with the most elevated ACE activities were more likely to have roentgenographic parenchymal disease and restrictive pulmonary function. Based on data collected from 12 international centers and nearly 2,000 patients, elevated ACE activity is expected in about 60 percent of subjects.33 One investigator, however, has reported increased ACE activity in 87 percent of cases of active sarcoidosis, but in only 9 percent of those with inactive disease.34 While elevated ACE activity is not diagnostic of sarcoid, it is useful in monitoring the clinical course of the disease on an individual patient basis.

Clinical evidence of myocardial sarcoidosis occurs in about 5 percent of cases, although autopsy data would suggest greater involvement (up to 20 to 27 percent).35 It may precede any of other more usual clinical manifestations or appear years after disease onset. The most frequent sign of myocardial sarcoidosis is electrical conduction disturbances, followed by rhythm abnormalities.36-38 Only one of our patients had a documented conduction disturbance (first-degree AV block). Pulmonary hypertension, a well-recognized complication of sarcoid lung disease, is more commonly a result of long-standing parenchymal fibrosis.
rather than pulmonary vasculitis.\textsuperscript{36} Cor pulmonale was a chronic problem in one young woman who had had multisystem disease diagnosed at age 13 years. After absence of follow up for ten years, she was found to have evidence of cor pulmonale with characteristic ECG and ECHO changes that have persisted over time.

The value of echocardiography in myocardial sarcoidosis is in detection of valvular disease, measurement of ventricular wall thickness, and documentation of septal and ventricular wall motion abnormalities.\textsuperscript{38} Our ECHO data were interesting in that seven patients had RVEDDs that exceeded established norms, four of whom had increased septal and posterior ventricular wall thickness. Three other subjects had borderline elevations of their RV end-diastolic dimension and septal and posterior wall measurements. An increased RV diastolic diameter with or without septal wall thickening or motion abnormality is suggestive of pulmonary hypertension and pressure overload of the right ventricle; similar ECHO findings have been documented in cases of chronic pulmonary hypertension due to primary pulmonary hypertension and in patients with acute pulmonary hypertension from pulmonary emboli.\textsuperscript{37-39} The significance of our data is unknown. The possibility that early sarcoid lung involvement may result in subtle, chronic changes in right ventricular anatomy warrants further investigation.

While anemia (less than 11.0 g/dl) is observed in approximately 5 percent of patients with sarcoidosis,\textsuperscript{30} none of our subjects was anemic. Elevated sedimentation rates occur in two thirds of individuals with sarcoid, especially in association with acute disease and erythema nodosum.\textsuperscript{32} Only one patient had a modestly elevated sedimentation rate in our series.

Hypercalcemia in sarcoidosis (estimated overall incidence, 11 percent) is usually transient in subacute disease and may fluctuate in the chronic state depending on disease activity. It is believed to result from endogenous overproduction of calcitriol with a secondary increase in intestinal calcium absorption.\textsuperscript{33} One of our subjects had a serum calcium level of 11.1 mg/dl. A 24-h urine collection, however, remains a more sensitive marker for the disordered calcium metabolism of sarcoidosis as hypercalcemia may be present without concomitant hypercalcemia.\textsuperscript{34} Routine renal function tests (creatinine, serum urea nitrogen) and urinalyses are not particularly helpful in assessing sarcoid activity in the absence of known renal disease.\textsuperscript{34}

Another well-described biochemical marker of sarcoidosis is hyperglobulinemia; it was observed in 23 to 96 percent of patients in a large international study.\textsuperscript{40} The serum IgG was elevated in more than half the subjects, serum IgA in one fourth, and serum IgM in approximately 15 percent. When sarcoid becomes inactive, IgG and IgM levels tend to fall, but IgA levels remain elevated.\textsuperscript{34} Of interest, five (26 percent) of our patients had IgA values above the norm for age and race, including two individuals with values of 1,000 mg/dl or greater.

Lymphopenia is a frequent finding in active sarcoidosis and represents an absolute reduction in the number of T cells.\textsuperscript{40} Although four of our adults still had active, chronic disease, none had reduced T cells by enumeration techniques. The absolute number of B cells in the peripheral blood may increase, decrease, or remain normal in active sarcoidosis.\textsuperscript{40} All B-cell counts were normal except in one individual with slightly low B-cell values compared with control subjects.

Due to depression of delayed-type hypersensitivity, patients with sarcoid often show cutaneous anergy to tuberculin and other bacterial, fungal, and viral antigens. This is believed to be related to excessive T-suppressor cell function in circulating T lymphocytes.\textsuperscript{40,41} Five of our patients were anergic to both tuberculin and monilial antigens. This particular immunologic defect may persist despite clinical and radiologic recovery.\textsuperscript{41,42} Individuals with sarcoid who develop active tuberculosis will react to tuberculin skin testing, but such reactivity may fade within several months.\textsuperscript{41} Active tuberculous infection should be suspected in any patient who develops a positive skin test, especially if receiving corticosteroid therapy.

The most significant long-term morbidity and mortality associated with sarcoidosis are related to the effects of the disease on the lungs.\textsuperscript{1,18} Moderate to severe loss of lung function was observed in four individuals at reexamination in 1985 (21 percent); three were considered to have chronic, ongoing disease. Five patients suffered nonpulmonary sequelae (26 percent). Of the initial 61 children and adolescents with sarcoid identified at our institution, five deaths were reported. Two deaths were from nonpulmonary causes, while details surrounding the other three cases are not known. These morbidity and mortality figures are in agreement with findings from other tertiary care centers.\textsuperscript{15,16,18,30,22,32} Some adult data suggest that less severe sequelae are observed in patients from community-based medical practices, but this probably reflects a less severely affected population.\textsuperscript{3}

It appears, then, that the long-term outcome of pediatric sarcoidosis is not significantly different from that of adult-onset disease, yet much information is lacking on the effects of this disorder on the developing child and young adolescent. The true incidence of the disease in the pediatric age group is unknown, pulmonary function data are often inadequate in younger patients, and long-term follow-up is complicated by a mobile society, transition to adult care providers, and
the benign outcome of the vast majority of affected individuals.

ACKNOWLEDGMENTS: We wish to express our appreciation to W. Bradford, M.D., for review of the pertinent biopsy slides of our patients; to J. Lieberman, M.D., for the determination of ACE activities; and to B. H. Buckley, M.D., for immunoglobulin levels and B- and T-cell enumerations. We also express our appreciation to Carol Lennon for the preparation of the manuscript.

REFERENCES

3 Reich JM, Johnson RE. Course and prognosis of sarcoidosis in a non-referral setting. Q J Med 1984; 78:61-7
13 Schill RI, Buckley RH, Gilbertsen RB, Metzger RB. Membrane receptors and in vitro responsiveness of lymphocytes in human immunodeficiency. J Immunol 1974; 112:376-86
22 Heatilington SV. Sarcoidosis in children. Compr Ther 1982; 8:63-8
37 Goodman DJ, Harrison DC, Popp RL. Echocardiographic features of primary pulmonary hypertension. Am J Cardiol 1974; 33:438-43