Intrathoracic Sarcoidosis*
A Review of 69 Cases

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"The study of causes of things must be preceded by the study of things caused." . . .
Hughlings Jackson

Despite advances in our knowledge of sarcoidosis, many aspects of the disease, such as etiology and pathogenesis, remain perplexing and controversial. A number of reviews of the clinical aspects of sarcoidosis have appeared in recent years. Considerable attention has been devoted to its natural history and prognosis. The literature is replete with articles dealing with unusual manifestations of the disease. Hypotheses and evidence regarding its possible causes have been offered.

This article reviews certain aspects of the disease in a group of 69 persons diagnosed as having intrathoracic sarcoidosis with or without extrathoracic disease in the period 1955 through 1961 at Henry Ford Hospital.

Diagnosis of Sarcoidosis

There is no unanimity among students of the disease regarding the definition of sarcoidosis. Participants at the 1960 International Conference on Sarcoidosis defined it as "a systemic granulomatous disease of undetermined etiology and pathogenesis," then went on to describe certain salient clinical, pathologic and laboratory features of the disease.

Sarcoidosis is difficult to define in clinical terms alone because of its protean, and frequently nonspecific manifestations and because of controversy over such points as the tuberculin test reactivity. Most students of the disease favor diagnosis based on the recognition of a consistent clinical picture taken in conjunction with characteristic pathologic findings of epithelioid cell tubercles with little or no necrosis found in excised lymph nodes, skin, liver, lung or other involved organs. Such tissue should be cultured and examined with special stains for tubercle bacilli and fungi. Most authorities hold that the sarcoid reaction is a non-specific one which can at times be found in tuberculous or fungus infection, beryllium disease and in association with malignant neoplasms. Of great interest is the fact that sarcoidosis tissue has been cultivated and shows a characteristic picture, offering a potentially useful tool for its study.

Scadding has criticized attempts to include in the definition of sarcoidosis the phrase that it is "a disease of unknown etiology" since this logically excludes any case in which a possible cause for the sarcoid process such as the tubercle bacillus is found; he defines the disease in terms of histology alone. However, to allow that any condition in which the sarcoid process is found is the disease sarcoidosis poses the threat that sarcoidosis may become "a formless monster without limits." Whether the disease is really a single entity or simply "a monomorphic tissue reaction elicited by different causes" remains an unsettled question.

Selection of Patients

After careful review of medical records and radiographs, a total of 69 persons were considered to have had intrathoracic (lung or lymph node) sarcoidosis diagnosed in the years 1955 through 1961 at our hospital. The basis of the diagnoses was a combination of clinical, radiographic and histologic evidence in nearly every case. Some persons diagnosed as having had sarcoidosis were excluded from this review either because of lack of intrathoracic manifesta-

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tions or because of a lack of sufficient information about them.

In view of the emphasis, particularly in Europe, that erythema nodosum may be a manifestation of sarcoidosis in certain cases, all 76 cases at our hospital indexed as having had erythema nodosum in the years 1955 through 1961 were reviewed. Three of 13 cases of erythema nodosum with hilar lymphadenopathy were considered to have had adequate study and to be examples of sarcoidosis and are included in the present series.

AGE, SEX AND RACE

The 69 subjects include 49 white persons (16 men and 33 women) and 20 Negroes (11 men and nine women). Differences in the disease in the white and Negro were not striking, although a disproportionate number of cases with hilar lymphadenopathy alone were seen in white subjects. Negroes tended to have a higher incidence of skin and eye involvement and disability due to the disease.

The ages of the subjects at the time of diagnosis are shown in Fig. 1. One-half of the white subjects and more than two-thirds of the Negro subjects were under 40 at the time of diagnosis. There did not appear to be any particular difference in the type of disease in those under 30 and those over 50 years of age at the time of diagnosis.

OCCUPATION, RESIDENCE AND FAMILY HISTORY

Most of the women were housewives. Among the men were professional people, white collar workers, skilled and unskilled laborers and farmers. In several, there was a history of occupational exposure to chemicals, paint fumes or dusts. Duration of residence in various parts of the country could not be determined.

In eight persons, a member of the family had had tuberculosis. Both the extent of

<table>
<thead>
<tr>
<th>Table 1—Physical Signs in 69 Persons with Sarcoidosis</th>
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<tr>
<td>Enlarged lymph nodes</td>
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<tr>
<td>Rales, rhonchi or wheezes</td>
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<tr>
<td>Hepatomegaly</td>
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<tr>
<td>Skin lesions</td>
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<tr>
<td>Pulmonary restriction</td>
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<tr>
<td>Eye lesions</td>
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<tr>
<td>Splenomegaly</td>
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<tr>
<td>Erythema nodosum</td>
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<tr>
<td>Signs of hypopituitarism</td>
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<tr>
<td>Accentuated P</td>
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<tr>
<td>Parotid enlargement</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
</tr>
<tr>
<td>Bell’s palsy</td>
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<td>Cerebellar signs</td>
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Figure 1: Age at the time of diagnosis in 69 persons with sarcoidosis.
contact between the sarcoidosis subjects and their tuberculous relatives and the time span between the occurrence of the two illnesses were difficult to ascertain. Six had relatives with “asthma” or chronic nontuberculous respiratory disease, and two had a relative with proved lung cancer. Two siblings, a brother and sister each with sarcoidosis, are included in this series. Recently, the brother of another subject was found to have noncaseating granulomas in a scalene lymph node biopsied because of the presence of hilar lymphadenopathy and a localized pulmonary infiltrate. Histoplasma capsulatum was cultured from the node. Both sets of siblings were Negroes.

Duration of Symptoms Before Diagnosis

In nearly half of the group, 34 of 69, symptoms had been present for less than one year before the diagnosis was established. Eleven had had symptoms for one to three years and six for more than three years. In five, the duration was indefinite. The disease was discovered fortuitously during routine or mobile unit chest x-ray examination in 13 persons (19 per cent), none of whom had symptoms at the time the x-ray film was taken.

Presenting Symptoms and Signs

Symptoms were present prior to diagnosis in 81 per cent (56 of 69). The most common were cough (frequently nonproductive), fatigue, dyspnea, weight loss, fever and/or sweats, often in combinations.

Physical signs at the time of diagnosis are listed in Table 1.

<table>
<thead>
<tr>
<th>TABLE 2—Skin Test Results in Sarcoidosis</th>
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<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>PPD 1st strength (1 T.U.)</td>
</tr>
<tr>
<td>PPD int. strength (5 T.U.)</td>
</tr>
<tr>
<td>PPD 2nd strength (250 T.U.)</td>
</tr>
<tr>
<td>O.T. 1:10 dil.</td>
</tr>
<tr>
<td>Histoplasmin</td>
</tr>
<tr>
<td>Coccidioidin</td>
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<tr>
<td>Blastomycin</td>
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Laboratory Studies

Studies of serum proteins, serum calcium, and liver function were performed in a number of the subjects. All had hemoglobin determinations and white blood cell counts.

In 70 per cent of the subjects tested (39 of 56) the serum globulin exceeded 3 gm. per cent, and in 19 (34 per cent) it was greater than 3.5 gm. per cent. The highest globulin recorded was 5.9 gm. per cent. The gamma globulin fraction was most often involved.

In only three of 40 subjects tested were serum calcium values in excess of 11 mg. per cent. All three were between 11 and 12. Abnormal bromsulphalein (BSP) retention was found in 11 of 19 cases in which it was measured, and serum alkaline phosphatase was elevated in three of 20 cases. All three had ocular sarcoidosis, skin lesions and hilar adenopathy; two had cystic changes in the bones, two had pulmonary parenchymal disease and one had hepatosplenomegaly.

Low-grade anemia was not an uncommon finding. In three instances, it was of a significant degree. Bone marrow examination revealed no granulomas in any of the few cases in which it was done. Leukopenia below 4,000/mm.³ was noted six times. Monocytosis or eosinophilia was seen on occasion, and a raised erythrocyte sedimentation rate was rather common.

Many of the subjects had sputum or gastric washings cultured for tubercle bacilli at the time of initial study; all such studies were negative.

Skin Tests

In all but three subjects, intracutaneous skin tests were recorded. Results are shown in Table 2. In some, the test was recorded as simply positive or negative; when expressed in terms of induration, the test was considered positive if more than 6 mm. of induration were present after 48 or 72 hours.

Seventeen per cent (11 of 64) skin tested for tuberculosis gave positive reactions.
The number of positive histoplasmin skin tests was less than might be expected in residents in this part of the United States.

Of the eight subjects with a family history of tuberculosis, the skin test with PPD was positive in only one.

Five persons originally came under observation because of suspected pulmonary tuberculosis, all having radiographic changes suggestive of that condition. Four complained of cough, weight loss and fever; one with no symptoms had been found to have an abnormal chest x-ray film on routine examination. Two of the five suspects had positive PPD skin tests. Bacteriologic studies for tuberculosis in all but one were negative. The following case is an example:

**CASE 1**

F. D., a 43-year-old white housewife, experienced chest pain on two or three occasions. She developed a mild cough and fever, and was admitted as a tuberculosis suspect. Physical examination was normal, and she looked well. Chest x-ray examination (Fig. 2A) revealed extensive, dense upper lobe infiltrates with partial consolidation of the right upper lobe. All skin tests including second-strength PPD (250 T. U.) were negative. Numerous sputum cultures were negative for tubercle bacilli and fungi. Sedimentation rate was 46 mm./hr. Serum gamma globulin was 1.93 gm. per cent (normal up to 1.25).

Scalene node biopsy showed noncaseating epithelioid tubercles. Special stains and cultures of the nodes were negative for tubercle bacilli and fungi. Prednisone was begun and in two months, the chest x-ray film was nearly normal (Fig. 2B). The chest roentgenogram one year later showed only a few fine linear shadows in the upper lobes and she had no symptoms.

**Comments:** Extensive upper lobe disease suggested the possibility of tuberculosis. Negative skin tests, raised serum gamma globulin and noncaseating granulomas in the scalene nodes were consistent with sarcoidosis, and the process cleared quickly while corticosteroids were being administered.

Repeat skin tests were not often done on the subjects in this study, but in the course of follow-up, two persons, one originally negative to intermediate-strength PPD (5 T. U.) and the other negative to second-strength PPD, converted to positive reactions. Tubercle bacilli were not demonstrable in their sputa, but one was given prophylactic isoniazid while receiving prednisone for fever and progression of what was considered to be diffuse pulmonary sarcoidosis. The process resolved quickly.

**DIAGNOSTIC BIOPSIES**

Ninety-one biopsies were obtained from 68 subjects. Erythema nodosum lesions were biopsied in two persons. In another

![Figures 2A and 2B](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21394/)

**Figure 2A:** Case 1, F.D.: Initial radiographic appearance showing extensive upper lobe infiltrates and consolidation. **Figure 2B:** Case 1, F.D.: Chest radiograph two months later while subject was receiving prednisone. Some residual infiltration is seen in the upper lobes.
INTRATHORACIC SARCOIDOSIS

person non-caseating granulomas were found in a uterus removed for therapeutic reasons; and in two, post mortem examination confirmed the diagnosis of sarcoidosis. In nearly all in whom lymph node biopsies were done, attempts were made to culture tubercle bacilli and fungi from the tissue, but this proved unsuccessful in all but one instance.

The various tissue biopsies are listed in Table 3.

From one subject in whom bilateral scalene lymph node biopsies revealed changes interpreted as consistent with the sarcoid reaction a single colony of tubercle bacilli was eventually cultured. A summary of the case follows:

**CASE 2**

C. H., a 26-year-old white housewife, had noted excessive fatigue for six months and following a brief pleurisy-like pain had a chest roentgenogram thought to suggest tuberculosis. Previous films seven, three, and two years before had shown no change in left upper lobe scars. Physical examination revealed a small axillary node; fever was absent. Hemoglobin was 10.8 gm. per cent; white blood count, differential, sedimentation rate and albumin/globulin ratio were normal. Serum calcium was 9 mg. per cent. Intermediate-strength PPD skin test (5 T.U.) was positive. Four gastric washings were negative on culture for tubercle bacilli. Initial chest x-ray film showed bilateral hilar adenopathy and fluffy bilateral infiltrates; no cavity was seen. Right and left scalene node biopsies revealed changes consistent with sarcoidosis. One colony of *M. tuberculosis* was cultured from a node and caused typical tuberculous infection in guinea pigs. Roentgenographically, the disease reached its peak two months later, then resolved almost completely in another two months with no treatment whatsoever. Four years later, the chest film

**Table 3—Biopsy Specimens in 68 Persons with Sarcoidosis**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>No. with Noncaseating or Non-Granulomas</th>
<th>Normal Specific</th>
</tr>
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<tbody>
<tr>
<td>Scalene lymph node</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>Other superficial lymph node</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Skin</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Liver</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Lung</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Bronchus</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Hilar lymph node</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Lip</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Kveim test</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Figure 3:** Case 3, W.S.: Radiograph showing rounded mass on the right and paratracheal nodal enlargement. Other films confirmed the presence of large bifurcation area nodes.
was normal, the patient symptom-free and healthy.

Comments: The picture of hilar adenopathy and widespread "soft" pulmonary disease and scalene nodes containing noncaseating tubercles suggested sarcoidosis, especially when the radiograph cleared rapidly and no treatment was given. The positive PPD skin test and culture of tubercle bacilli from a lymph node suggests that this case may be an example of the sarcoïd process (sarcoidosis?) related to tuberculous infection.

Multiple diagnostic biopsies were performed in 22 persons.

The following case illustrates the usefulness of multiple biopsies:

CASE 3

W. S., a 57-year-old white man woodworker, complained of fatigue, anorexia and weight loss for three months, and later of productive cough. Examination revealed a few supraclavicular nodes. The spleen tip was palpable on inspiration. Chest roentgenogram (Fig. 3) showed a lobulated mass 6 cm. in diameter in the right lower lobe adjacent to the major fissure and a large mass of nodes in the bifurcation area and paratracheal region. Skin tests, including second-strength PPD, were negative. Hemoglobin was 8.5 gm. per cent. Bone marrow examination showed normoblastic hyperplasia. White blood count was 8,050 per mm.³ with a left shift. Serum gamma globulin was 2.35 gm. per cent. Bronchoscopy revealed some narrowing of the right lower lobe bronchus; bronchial biopsy was unrevealing. Liver biopsy was normal. Supraclavicular lymph node biopsy showed granulomas with some necrosis. Special stains were negative for acid-fast bacilli and fungi. An axillary lymph node showed reactive hyperplasia; smears and cultures were negative. Thoracotomy was performed, and the mass in the right lung was thought to be a lymphoma on frozen section. Permanent sections of this and hilar lymph nodes resected showed a uniform pattern of granulomatous change with minimal necrosis. All studies for tuberculous and fungous infection were negative. The patient improved during treatment with corticosteroid therapy. A year later, he was admitted to another hospital where he was found to have hepatosplenomegaly. The chest x-ray film revealed a right hilar mass. Diabetes mellitus was present. Hemoglobin was 6.1 gm. per cent, the indirect bilirubin 1.3 mg. per cent with a total of 1.8, reticulocyte count 15 per cent, Coombs tests (indirect and direct) were positive and red cell survival studies showed an increased rate of destruction in the region of the spleen. A splenectomy was performed and the specimen showed changes consistent with sarcoidosis, but the pathologist raised the question of an occult lymphoma. Postoperatively, the reticulocyte count dropped to normal, but the anemia responded poorly. Corticosteroids were continued, the patient lost weight, became weaker and died within half a year. A necropsy was not performed.

Comments: Despite the several biopsies which were felt to be consistent with the sarcoïd process, and fruitless efforts to establish the diagnosis of tuberculosis or fungus infection, the roentgenographic appearance of the disease, the relentless course unaffected by corticosteroids, and the severe hemolytic anemia all cast doubt on the diagnosis of "typical" sarcoidosis. Numerous reports are to be found in the literature describing noncaseating granulomas in regional lymph nodes in persons harboring a malignant neoplasm. Moreover, cases have been reported in which a diagnosis of sarcoidosis was first made, the disease later to be "complicated" by the appearance of Hodgkin's disease or another lymphoma. Acquired hemolytic anemia has been reported in sarcoidosis, but only rarely.

In four subjects, the only biopsy performed gave indefinite results. These included three lymph node biopsies and one skin biopsy. In one person the only biopsy confirmed the diagnosis of erythema nodosum.

Where multiple biopsies, including scalene node were performed, the latter was consistent with sarcoidosis in 13 of 15 cases. In the remaining two cases, lung biopsy was the second biopsy and revealed epithelioid tubercles both times. Altogether the biopsy accompanying a scalene node biopsy was abnormal in 10 of 15 instances. Scalene node examination was abnormal in 40 of 44 cases and was equally helpful regardless of the roentgenographic picture of the disease in the chest. Biopsy of cervical, axillary or epitrochlear lymph nodes revealed epithelioid tubercles in nine of 15 cases.

INITIAL ROENTGENOGRAPHIC APPEARANCE

The roentgenographic appearance of the disease in the chest at the time of diagnosis can be classed as one of three types: (1) hilar with or without mediastinal lymphadenopathy; (2) pulmonary parenchymal disease only, and (3) a combination of the above types.
The picture of hilar and mediastinal adenopathy is well known. Pulmonary disease in sarcoidosis may have a variety of appearances, being either local or widespread in distribution. The lesions may range from finely granular or miliary shadows to coarse macro-nodules, or may appear as linear or soft infiltrative shadows. In the more chronic phase, roentgenographic signs of fibrosis, bullae, and emphysema may appear.

The roentgenographic appearance at the time of diagnosis of the disease in the present series is summarized in Table 4.

<table>
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<th>Table 4—Roentgenographic Appearance in Sarcoidosis</th>
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<tr>
<td>Initial Appearance</td>
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<tr>
<td>Hilar adenopathy</td>
</tr>
<tr>
<td>Hilar adenopathy and pulmonary disease</td>
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<tr>
<td>Pulmonary disease</td>
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Roentgenographic worsening in the hilar adenopathy group consisted of the development of pulmonary disease, usually widespread, with or without change in the hilar adenopathy. Progression in the other categories implied increased pulmonary shadows at times suggesting fibrosis, or the development of emphysematous changes or cysts. The follow-up roentgenograms indicated a significant number in whom no change or progression of disease was noted. Since the average follow-up period was only several years these figures must be viewed cautiously.

Of the 13 subjects who were asymptomatic at the time the disease was detected by routine chest roentgenography, six were found to have hilar adenopathy, six had hilar adenopathy with pulmonary disease, and one had pulmonary disease alone.

Five subjects had erythema nodosum. All had hilar lymphadenopathy; two had associated pulmonary disease, one upper lobe fibrosis, the other diffuse nodular disease.

In general, it may be said with respect to the present series that the subjects with hilar adenopathy alone were less likely to have symptoms than those who had pulmonary involvement.

**Pulmonary Function Studies**

Only a small number of subjects, 19 (28 per cent), underwent tests of pulmonary function. Nearly four-fifths showed defects of some type, but the subjects were not randomly chosen. Two with hilar adenopathy had normal ventilatory tests (vital capacity, timed vital capacity, and maximum breathing capacity). Of 17 with pulmonary disease with or without hilar adenopathy, two had normal studies, 11 of the remaining 15 had a restrictive defect (diminution in the vital capacity), and eight had an element of obstruction denoted by a decrease in the timed vital capacity and decrease in maximum breathing capacity. Arterial oxygen unsaturation was present in six, but not all subjects had blood gas determinations. The following case presents interesting aspects of pulmonary function, particularly as related to radiographic changes.

**Case 4**

A. E., a 47-year-old white clerk, had a dry "cigarette" cough, dyspnea during mild exertion, and a feeling of chest tightness. On examination, fine rales were heard in his lower lung fields, chest expansion was poor and respirations were rapid. Chest x-ray films (Fig. 4A and B) showed diffuse finely nodular and reticular shadows with prominent hila. All skin tests were negative. Sedimentation rate was 34 mm./hr.; peripheral blood smear showed 12 per cent monocytes; serum gamma globulin was 1.77 gm. per cent. Vital capacity was 2.91 L. (73 per cent of predicted), the 3 second volume was 87 per cent and the maximum breathing capacity was 123 L./min. (85 per cent of predicted). Resting arterial oxygen saturation was 84 per cent, and the arterial pCO2 was 38 mm.Hg. During exercise, there was marked hyperventilation. Lung biopsy through a "small" incision showed noncaseating granulomas. Special stains and cultures of lung tissue were negative for tubercle bacilli and fungi. Prednisone was begun, symptoms were remarkably and rapidly relieved, and the vital capacity improved; the x-ray film showed complete clearing. After ten months, prednisone was

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lymph node involvement, were demonstrable.

Skin sarcoidosis was diagnosed in nine persons, eye involvement in six, and bone disease in three of 20 in whom films of the hands were taken. One person presented with Bell's palsy. Two persons had evidence of pituitary disease. One was a young woman whose hypopituitarism affected gonads and thyroid predominantly. The other was a young man with panhypopituitarism. A summary of his case follows:

CASE 5

A. G., a 19-year-old Negro, had been bothered by headaches, fatigue, weight loss, polydipsia and polyuria, and impotency for two years. Studies elsewhere revealed diffuse pulmonary changes and hilar adenopathy on chest x-ray examination, and negative studies for tuberculosis. On examination, some small nodes were felt in the neck and axillae; prostate and testes were small and the pubic hair pattern was female in type. Chest x-ray examination at this time showed an extensive, soft, nodular process in both lungs. All skin tests were negative. Serum albumin was 3.83 gm. per cent and globulin 5.1 gm. per cent (gamma globulin 2.3). Skull x-ray films were normal. A Hickey-Hare test was diagnostic of diabetes insipidus; urinary steroid studies were diagnostic of adrenal-cortical insufficiency; $^{111}$ uptake was 11 per cent in 24 hours. A suprACLavicular lymph node revealed noncaseating epithelioid tubercles; cultures were negative for tubercle bacilli and fungi. Treatment with posterior pituitary snuff, thyroid, testosterone and prednisone (7.5 mg./day) affected relief of all symptoms; marked clearing of the chest x-ray film occurred simultaneously.

Comment: Diabetes insipidus is occasionally seen in sarcoidosis. Panhypopituitarism is much less common. Only a few cases have demonstrated recovery from diabetes insipidus following corticosteroid therapy.

In three persons multiple systems besides lungs were involved (skin and bone; skin, eye and bone; and skin, eye, bone, parotid and probably liver, heart and kidney). The following case illustrates widespread disease:

CASE 6

J. J., a 26-year-old Negro, had a productive cough, fever, sweats, and lost weight. He noted skin lesions, burning of his eyes, nasal stuffiness, nocturia and polyuria. His sister was known to have sarcoidosis. On examination, generalized

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**Figure 4A (upper):** Case 4, A.E.: Initial radiograph showing a diffuse finely nodular and reticular process. **Figure 4B (lower):** Case 4, A.E.: Detail view of the diffuse process.

stopped; within two months, symptoms, roentgenographic and ventilatory abnormalities recurred, and again responded quickly during administration of prednisone.

Comment: The quick relapse after cessation of ten months of corticosteroid therapy suggests that in some instances the drug may be required for prolonged periods to suppress the disease.

**Extrathoracic Sarcoidosis**

In 16 of the 69 subjects (23 per cent), both intrathoracic and extrathoracic sarcoidosis, exclusive of liver or superficial
lymphadenopathy, enlarged parotid glands and numerous cutaneous sarcoids were present; conjunctival follicles, band keratitis, and retinal sarcoids were noted by the ophthalmologist. Chest roentgenogram revealed mild generalized cardiomegaly, hilar adenopathy, and a diffuse nodular infiltrate in the lungs. Films of the hands showed cystic changes of sarcoidosis. Hemoglobin was 10.5 gm. per cent; sedimentation rate was 36 mm./hr.; peripheral blood smear revealed 16 per cent monocytes; BSP test was negative; alkaline phosphatase was 7.2 Bodansky units, serum gamma globulin 3.29 gm. per cent, serum calcium 11.8 mg. per cent, and blood urea nitrogen 30 mg. per cent. Scalene node and lip biopsy revealed noncaseating granulomas. Prednisone therapy was begun but follow-up was inadequate.

There appeared to be no particular pattern of disease in the chest radiograph in persons with extrapulmonary sarcoidosis. Eye and skin manifestations were more common in Negroes than in whites.

**Disability and Death**

Some of the subjects with ventilatory abnormalities, as well as a number not studied by pulmonary function tests, were considered to have had a certain degree of disability imposed on them as a result of their disease.

Five persons are known to have died; two from respiratory and cardiac insufficiency, one from multiple pulmonary emboli, one from pneumonia following an overdose of barbiturates, and one from unknown causes. Four of these persons had previously been found to have restrictive ventilatory impairment suggesting fibrosis. Four had diffuse lung disease, and one had multiple large pulmonary nodules.

**Follow-Up Period**

In 19 patients, no follow-up was obtained after the initial study. In 18, the follow-up period was two years or less at the end of 1961. In 18, it was from two to four years, and in 14 from four to six years.

**Discussion**

Because of obvious differences in composition of various series, no attempt will be made to compare in detail this with others. Certain points, however, seem worthy of discussion.

The presence of erythema nodosum as an initial manifestation of sarcoidosis in five of 69 patients represents an incidence of 7 per cent, higher than reported in several other American series, but lower than in others from England and Scandinavia. Two explanations seem possible—either erythema nodosum as a manifestation of sarcoidosis is indeed rare in this country or the association is being missed by clinicians. From the review of erythema nodosum cases previously referred to, it is the author's belief that more diligent study, especially skin testing and scalene node biopsy, in erythema nodosum cases with hilar adenopathy would yield a greater incidence of cases compatible with sarcoidosis.

Symptomatology in the present series conformed to the pattern in other series. A significant number of cases of sarcoidosis are first detected at the time of a routine chest x-ray examination. The most common symptoms in the present series—cough, fatigue, dyspnea and weight loss—called attention to a systemic or respiratory illness. Tuberculosis was not infrequently suspected because of symptoms and/or radiographic findings, and 17 per cent of the subjects had positive tuberculin tests.

Physical signs in the average case are not likely to be helpful. Eye or skin manifestations may be suggestive of the disease, but most physicians are probably poorly acquainted with them.

The initial roentgenographic appearance of the chest varies considerably in different series. Pulmonary involvement was seen in only 12 per cent of Ricker and Clark's cases, but in 87 per cent of Riley's (the former from the United States Army, the latter from a great metropolitan charity hospital). In the present series, 68 per cent had pulmonary involvement at the time of diagnosis. This wide range of figures probably results from the type of population served by the hospitals from which the dif-
ferent series emanate, and the vigor with which mass radiographic surveys are carried out in certain countries or groups.

Extrathoracic lesions were less common in the present series than in most others. Thirteen per cent had skin involvement, 9 per cent eye lesions, and 15 per cent bone lesions; but it should be recalled that by no means were all patients subjected to bone radiographs or expert ophthalmologic examination. Smellie and Hoyle found ocular sarcoidosis in 42 per cent of their patients, all of whom underwent special eye examinations.

As in many other series, the usefulness of scalene lymph node biopsy in the diagnosis of sarcoidosis was confirmed in the present study. Experience with liver biopsy was not extensive, but has been found to yield a high percentage of positive biopsies in sarcoidosis. Lung biopsy can be expected to yield a very high percentage of diagnoses when scalene node biopsy fails in subjects with pulmonary disease. Any suspicious skin lesion should, of course, be removed and examined.

Pulmonary function studies in sarcoidosis may show a variety of abnormal patterns. Both restrictive and obstructive phenomena may be seen, the latter perhaps related to bronchial or bronchiolar disease. As a matter of fact, bronchial biopsy to demonstrate noncaseating tubercles has been recommended as a diagnostic aid. Arterial blood gas disturbances and diffusing capacity reduction may be seen in certain cases. These studies are best employed serially in attempts to correlate with radiographic changes and effectiveness of therapy.

In the present series, 32 patients were followed two or more years after diagnosis. Of 13 with hilar adenopathy at the time of diagnosis, five showed roentgenographic worsening during follow-up. Of ten with hilar adenopathy and pulmonary disease, eight were either unchanged or worse. Of nine with pulmonary disease alone, eight were unchanged or worse at the end of follow-up. European, English, and some American observers have pointed out the benign nature of sarcoidosis manifested by hilar adenopathy, but Sones and Israel found no significant difference in the behavior of various radiographic types.

Without long follow-up periods the course of the disease and effectiveness of treatment, namely by corticosteroid hormones, is difficult to ascertain. The author believes that these drugs should be used in persons with significant symptoms or pulmonary function abnormalities and in cases with widespread pulmonary disease, especially if there is evidence of progression. Treatment should be given on a long-term basis. Cases with hilar lymphadenopathy alone can be observed without treatment. There is general agreement that active ocular sarcoidosis, progressive pulmonary involvement, persistent hypercalcemia or hypercalciuria, significant central nervous system disease, disfiguring skin lesions or myocardial damage all are indications for corticosteroid therapy.

**SUMMARY**

In a series of 69 cases of intrathoracic sarcoidosis diagnosed between 1955 and 1961, the diagnosis was generally made on the basis of a consistent clinical picture, roentgenographic findings of hilar lymph node enlargement and/or pulmonary involvement and the finding of noncaseating epithelioid tubercles in biopsied tissue.

The most common symptoms were cough, fatigue, dyspnea, weight loss, and fever or sweats. One-fifth had no symptom at the time of diagnosis.

Elevation of serum globulin, particularly the gamma fraction was the most consistent laboratory abnormality.

Eight subjects had a close relative who had had tuberculosis. In 17 per cent of 64 cases, the tuberculin test was positive. In only three of 47 was the histoplasmin skin test positive.

Ninety-one biopsies were made in 68 subjects. Scalene node biopsy revealed epithelioid tubercles in 40 of 44 cases in which it was done.
A variety of pulmonary involvement was seen, including local and widespread disease, ranging from fine to coarse shadows. Evidence of no change or progression of disease was noted in 21 of 32 with a two-year or more follow-up.

Five of the 69 subjects had erythema nodosum.

Pulmonary function abnormalities included both restrictive and obstructive phenomena and blood gas abnormalities.

Extrathoracic sarcoidosis (exclusive of liver or lymph nodes) was demonstrated in nearly one-fourth of the subjects, more often in Negroes.

Five persons are known to have died, four from cardiopulmonary causes.

**Resumen**

En una serie de 69 casos de sarcoidosis diagnosticados entre 1955 y 1961 se hizo el diagnóstico generalmente sobre la base de un cuadro clínico consistente, hallazgos radiográficos de crecimiento ganglionar hilar y/o invasión pulmonar y los hallazgos de tuméculos epitelioides no caseificados en los tejidos de biopsia.

Los síntomas más comunes fueron: tos, fatiga, disnea, adelgazamiento, fiebre y sudores. Un quinto de los casos fueron asintomáticos.

Ocho de los enfermos tenían un pariente cercano con tuberculosis. En 17 de 64 casos la reacción tuberculínica fue positiva. En sólo tres de 47 casos la reacción cutánea a la histoplasmina fue positiva. Se hicieron 91 biopsias en 68 enfermos. La biopsia de los ganglios escalenicos reveló tuméculos epitelioides en 40 de 44 casos en que se hizo.

Se observó una variedad de lesiones pulmonares, incluyendo la enfermedad local y la diseminada, desde manchas finas hasta gruesas. Se vie que hubo cambio progresivo en 21 de 32 a los dos años de observación. Cinco de 69 enfermos tuvieron eritema nudo. Las anormalidades de la función pulmonar incluyeron fenómenos tanto restrictivos como obstructivos y anormalidades en los gases de la sangre. La sarcoidosis extratorácica (excluyendo el hígado o los linfáticos) se demostró en casi un cuarto de los enfermos, y más a menudo en los negros. Cinco personas fallecieron, cuatro de afecciones cardiopulmonares.

**Resumé**

Dans un groupe de 69 cas de sarcoidoses intrathoraciques, découverts entre 1955 et 1961, le diagnostic fut généralement basé sur un tableau clinique valable, sur des constatations radiographiques de volumineuses adénopathies hilaires et/ou d’atteinte pulmonaire et sur la constata
tion de tubercules épithélioides non sécrétants dans les tissus biopsiés.

Les symptômes les plus communs furent la toux, la fatigue, la dyspnée, la perte de poids et la fièvre ou la transpiration. Un cinquième des cas n’avaient aucun symptôme au moment du diagnostico.

L’élévation des globulines du sérum, particulièrement de la fraction gamma, fut l’anomalie biologique la plus stable.

Huit sujets avaient un parent proche qui avait eu une tuberculose. Pour 17% des 64 cas, le test tuberculique fut positif. Pour trois seulement sur 47 cas, il y eut un test cutané positif à l’histoplasmine. 91 biopsies furent faites chez 68 sujets. La biopsie du ganglion scénique révéla des tubercules épithélioides pour 40 des 44 cas chez lesquels elle fut faite.

L’atteinte pulmonaire se caractérisait par des lésions localisées ou disséminées allant depuis des ombres très fines jusqu’à des images volumineuses. L’absence de modification ou d’extension de l’affection fut note dans 21 des 32 cas qui furent suivis pendant deux ans ou plus.

Cinq sujets sur 69 eurent un érythème noueux.

Les anomalies de la fonction pulmonaire comprenaient des phénomènes à la fois restrictifs et obstructifs et des anomalies des gaz sanguins. Une sarcoidose extrathoracique (à l’exclusion du foie ou des ganglions lymphatiques) fut mise en évidence dans près d’un quart des sujets, plus souvent chez les Noirs. L’auteur a appris le décès de cinq personnes dont quatre par atteinte cardiovasculaire.

**Zusammenfassung**


Die am häufigsten vorkommenden Abweichungen bei den Laboratoriums-untersuchungen bestanden in einer Erhöhung des Serums Globul, besonders ihrer Gammafraktion.

8 Patienten hatten enge Verwandte, die an Tuberkulose gelitten hatten. In 17% der 64 Fälle war der Tuberkulintest positiv. In nur 3 der 47
Fälle war der Histoplasmin-Hauttest positiv. 91 Biopsien wurden bei 68 Personen durchgeführt. Die Scalenus-Lymphknotenbiopsie ergab Epitheloidzellentuberkel bei 40 von 44 Fällen, bei denen sie ausgeführt worden war.

Es wurde eine Vielfalt pulmonaler Veränderungen beobachtet, einschließlich dissemierter Krankheitsformen schwankend zwischen feinen und grobkörnigen Verschattungen. Anhaltspunkte für fehlende Veränderungen oder Fortschreiten der Erkrankung wurde in 21 von 32 Fällen während einer 2 Jahre oder längerdauernden Beobachtung gewonnen. 5 der 69 Patienten hatten ein erythema nodosum.

AORTOPLASTY IN COARTATION

Surgical therapy was applied to 40 patients with coarctation of the aorta and in two patients with the occlusive syndrome of the aortic arch. The age of patients ranged from 16 to 30 years. In 30 patients, the affected aortic segment was resected and allopasty with the vascular prosthesis was utilized. Various plastic procedures including the use of the Teflon patch were applied to nine patients. In one case, the left subclavian artery prosthesis was sutured into the aortic prosthesis. In six patients, extracorporeal perfusion, and in one patient perfusion of the lower extremities with a bag-oxygenator was used. Indications to the use of extracorporeal perfusion in patients with this pathology are determined. Late results of the aortoplasty were followed up for six years.

For reprints, please write Dr. Bower, Henry Ford Hospital, Detroit.

CARDIOVASCULAR DISEASES IN DIABETES MELLITUS

Hypertension was present in 28.4 per cent of 922 diabetics. It occurred earlier and more frequently than among nondiabetics. Clinically demonstrable arteriosclerosis in diabetics, chiefly based upon fundoscopic findings, was present in 32.6 per cent. Hypercholesterolemia was detected in 27.3 per cent. The total incidence of cardiovascular diseases in diabetics, including hypertensive heart disease, coronary arteriosclerotic heart disease, cerebrovascular accidents, gangrene of extremities and skin, and diabetic glomerulosclerosis, was 11.2 per cent. Congestive heart failure often exacerbates the diabetic state and in certain cases, even leads to ketoacidosis. Excessive dosage of insulin causes hypoglycemia which is detrimental to the outlook of congestive heart failure. Excessive fluid therapy during the treatment of ketoacidosis in diabetics with subclinical coronary arteriosclerotic heart disease or poor myocardial reserve may precipitate congestive heart failure and should be avoided. The ECG will show abnormal findings only when diabetes is complicated by severe ketoacidosis with electrolyte disturbances (especially serum potassium), or associated with various cardiovascular complications including latent coronary arteriosclerosis.

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CONGENITAL AORTIC STENOSIS

Cardiac catheterization can probably be safely deferred in patients with congenital aortic stenosis, if they are asymptomatic and have no definite evidence of left ventricular hypertrophy on physical examination, no roentgenologic evidence of cardiac enlargement, or left ventricular hypertrophy with strain on the electrocardiogram. In the age group studied (3.5 to 32 years), the absence of a chest wall thrill was indicative of mild disease, even in the presence of "suggestive" symptoms or questionable changes on the chest x-ray and electrocardiogram. The authors recommend further evaluation of this sign, in larger series of patients, to determine its value as a screening aid. Positive indications of critical stenosis are left ventricular hypertrophy and strain on the electrocardiogram, or definite left ventricular enlargement on roentgenograms of the chest.

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