Acute and Subacute Disseminated Lupus Erythematosus

A Correlation of Clinical and Postmortem Findings in Eighteen Cases

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Eighteen cases of disseminated lupus erythematosus were verified by postmortem study in a series of 19,242 autopsies. Shortness of breath was the most common complaint and occurred in 16. Fourteen of this number had definite cardiac pathology. All 16 had definite pulmonary pathology. Fourteen cases had abnormal urinalysis. Of these cases, 7 had elevated blood nonprotein nitrogen values of over 40 mg., and only 4 had hypertension. However, 14 cases had abnormal pathologic renal findings. Fifteen of the 18 cases had a skin lesion; 11 of the 15 were definitely of the lupus type. Hypochromic anemia was present in 17, leukopenia in 14, elevated sedimentation rate in all cases recorded and an elevated serum globulin in 9. The diagnosis is made by summation of the clinical findings; namely, shortness of breath, joint pains, skin rash, fever, pulmonary, cardiac, and renal abnormalities, and by the laboratory findings of hypochromic anemia, albuminuria, increased sedimentation rate, elevated serum albumin, presence of lupus erythematosus cells, and by a positive skin biopsy.

Lupus erythematosus was first described by Hebra as a cutaneous disease and was named "seborrhea congestiva," in 1845. Six years later Cazenave gave the disease its present name because he thought that it was an erythematous form of "lupus" which later was considered as a form of cutaneous tuberculosis. In 1872 Kaposi pointed out that the disease sometimes had systemic reactions and was at times fatal. The clinical features of the disease were clarified by Jadasohn and later by Osler. In 1924 Libman and Sacks described a nonbacterial verrucous endocarditis which involved the cardiac valves and the mural endocardium. Subsequent studies have shown that vascular lesions involving vascular endothelium and subendothelial tissue and similar lesions of the serous membranes were common in the latter condition and in lupus erythematosus. According to Baehr, Klemperer and Schifrin, in both diseases typical changes in the blood vessels were widely disseminated throughout the body. Guion and Adams concluded that disseminated lupus erythematosus is primarily a diffuse vascular disease affecting chiefly small arteries and arterioles. Klemperer believes that acute lupus erythematosus is a disease characterized by a fundamental alteration of the collagen portion of the connective tissue.

Today most investigators agree that lupus erythematosus has no connection with the tubercle bacillus. The real etiology of the disease is unknown. Some British authors have become convinced that hemolytic streptococci are responsible for the disease. Others have claimed allergy to be the cause. However, Baehr and Pollack are opposed to this idea.

The fundamental pathologic process takes place in the connective tissue. All elements of this tissue are injured. The vascular changes are similar no matter where they occur. The edema and fibrinoid degeneration in the subendothelium is followed by endothelial proliferation leading ultimately to thrombosis. There are frequently collections of lymphocytes and fibroblasts in and around the adventitia and in the media. The heart is frequently enlarged. Atypical verrucous endocarditis is now thought to be a local variant of the disease. Fibrinoid degeneration may also affect the mural endocardium with the formation of small vegetations. The mitral valve is most commonly affected.
The valves are richly vascularized. In addition, the myocardium often shows foci of segmental leukocytes but Aschoff bodies have not been described. The cardiac lesions were analyzed by Humphreys.10 Twelve cases had endocardial lesions and most of the cases showed some focal myocarditis. In 9 cases a serofibrinous pericarditis was present. In this condition the spleen reveals a peculiar periartrial fibrosis confined to the central and pericillary arteries, which was first described by Libman and Sacks. In microscopic examination, a thick collar of connective tissue is seen around the central arteries and resembles "onion skin." According to Tei- lum,8 the hyperglobulinemia and periartrial fibrosis occurring in the spleen in lupus erythematous are identical pathogenetically and morphologically with the alteration in Boeck's sarcoid and the atypical amyloidosis, having allergic hyperglobulinosis as the common primary foundation. Another lesion of frequent occurrence is the special alteration of the glomerular coils of the kidneys which has been characterized as "wire loops" by Baehr, Klemperer and Schifrin2 because of the resemblance of the coils to bent wire. According to Klemperer, Pollack and Baehr,4,9 the coils are irregularly thickened and rigid, and strongly eosinophilic. In other cases, there is focal fibrinoid necrosis of part of the glomerular coils, the others remaining unaffected.

The disease is most common in the third decade of life. However, patients under the age of 30 years have been reported in the literature.11 Less than 5 per cent of the cases are males. Dermatologists12 recognize four types of lupus erythematosus: (1) the localized or chronic discoid type, (2) the generalized discoid type, (3) the subacute disseminated type, and (4) the acute disseminated type. The discoid type is not associated with visceral vascular and endothelial lesions. The course of subacute type is characterized by intermissions between exacerbations. During these intermissions the patient has no symptoms. On the other hand, the acute type has no interruption at all, or, if any, only incomplete and short-lasting. The clinical manifestations in acute disseminated lupus, with their frequency, have been listed as follows by Montgomery13: fever, in 97 per cent; anemia, in 84 per cent; leukopenia (less than 4,000), in 71 per cent; arthralgia or arthritis, in 63 per cent; and albuminuria, cylindruria and microscopic hematuria, in 32 per cent of the cases. One of the most constant signs is fever. It may be accompanied by chills and profuse sweats. Tachycardia is proportional to the degree of temperature. The cutaneous lesions are merely the local manifestations of a systemic disease. They may involve almost any part of the body but particularly the face and fingers. Joint pain is a frequent occurrence. The arthritis often precedes cutaneous lesions, so that the early clinical picture may resemble and may be confused with both rheumatoid arthritis and rheumatic fever. Lymphadenopathy is generally considered to be common. Involvement of the serosal membranes with the formation of effusion is common late in the course of the disease. The signs and symptoms in regard to the cardiovascular system are neither constant nor characteristic of the disease. The total serum protein is usually within normal range, but hyperglobulinemia is reported to be a constant occurrence. Abnormalities of the urine are present in most cases but they are nonspecific. The persistence of the urinary findings with little evidence of progression over long periods suggests that they are a relatively mild reaction to some toxic process.14 Leukopenia with uniform reduction of all white cells is a feature of this disease. Recently a polymorphonuclear leukocyte containing an inclusion body was described in the peripheral blood and bone marrow of patients with acute disseminated lupus erythematosus. It is hoped that this cell (L.E. cell*) will be of

* The L. E. cell can be found by hiratinizing the bone marrow and after waiting for an hour it is located among the polymorphonuclear leukocytes. It may be found in the peripheral blood by centrifugation and observing the L. E. cells in the buffy coat. The L. E. cell cannot be differentiated at postmortem study because the hematoxylin bodies in the lymph glands have the same staining qualities. The actual composition of the lupus erythematosus cell is disputed. In our laboratory, we have been unable to find the L. E. cells unless the specimen has been exposed to sunlight. Specimens of blood examined in a darkened laboratory are negative while the same specimens when studied after a period of time in bright sunlight reveal the cells.
great help in the diagnosis of acute disseminated lupus erythematosus in cases exhibiting minimal clinical manifestations.14-17

**Purpose of the Study**

The purpose of this study is to correlate the clinical evidence with pathologic findings in 18 cases of acute and subacute disseminated lupus erythematosus. In review of this disease, special consideration and emphasis has been placed on the clinical and pathologic findings in the cardiovascular system. A careful review of the case studies was made and statistical compilations were recorded in order to correlate specific organ lesions with clinical manifestations due to the collagenous changes as well as noncollagenous lesions.

**General Observations**

**Clinical**

From 1939 through 1948, 17 cases of acute and subacute disseminated lupus erythematosus were verified by necropsies performed in the Los Angeles County Hospital; with one additional case taken from the files of the Birmingham Veterans Administration Hospital, a total number of 18 cases was studied. A total of 19,242 autopsies were performed. The average autopsy incidence of this condition during this 10 year period was 0.088 per cent. The youngest patient was 17 years of age, and the oldest was 64 years of age. Seventy-seven per cent were in the second and third decades. Seventeen patients were females and only one was a male. Thirteen of 18 cases were Caucasians, 3 were Negroes and 2 were Mexicans.

Joint pains were the most common among the chief complaints of the patients and were encountered in 13 cases. The typical butterfly rash occurred in 11, cough in 6, chest pain in 4, nausea and vomiting in 3, nosebleeds in 1, and vaginal bleeding in 2 patients. Of 13 cases with joint pains, 2 had not had any skin lesions; and of 15 cases with some kind of skin lesion, joint pains preceded skin manifestations by 5, 11, and 12 months, respectively. In each of the 18 cases the pulse rate was above 100 per minute, and each had a high temperature at some time during his illness. Six of 18 cases had ankle edema, but this occurred rather late during the course of the disease. The important findings in the past history of these cases are shown in table 1.

**Laboratory**

Seventeen of the 18 cases had a hypochromic anemia, in 6 of which the erythrocyte counts were between 2.2 and 3 million per cu. mm.

Fourteen cases had leukopenia. In 4 of these cases the leukocyte count was below 3000; in 5, below 4000; in 2, below 5000 and in 3 cases, below 6000 per cu. mm. In 2 cases, the leucocyte counts were normal and in the other 2 cases slight elevations were noted; 10,000 and 12,000, respectively.

Erythrocyte sedimentation rates were determined in 5 cases. All had a rate between 15 and 41 in the first 60 minutes.

The albumin-globulin ratio was determined in 13 cases. Two of these, had a total serum protein below 5 Gm. In 9 of the 13 cases the globulin determinations of the serum were above 2.5 Gm. and in 2 other cases they were below this amount.

Wassermann and Kahn reactions were negative in all patients.

**Cardiovascular System**

**Clinical Data.** Sixteen of 18 cases complained of shortness of breath, but this symptom occurred rather late during the course of disease.
Chest pain was among the chief complaints in 4 of the patients.

Of 17 cases in which blood pressure measurements were recorded 4 showed a diastolic pressure of more than 90 mm. Hg; the highest reading was 240/140.

Three of the 17 cases had a clinically detectable left ventricular enlargement. Apical systolic murmurs were present in 7, a late diastolic rumble in 1, aortic systolic murmur in 1, and an early diastolic murmur in 1 case. Pericardial effusions were diagnosed clinically in 2 cases. Each patient had a regular pulse.

**Table 2.—Reported Causes of Death in Eighteen Cases of Acute and Subacute Disseminated Lupus Erythematosus**

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Cases</th>
</tr>
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<tbody>
<tr>
<td>Number</td>
<td>Per cent</td>
</tr>
<tr>
<td>--------</td>
<td>-----------</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>5</td>
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<tr>
<td>Lobar pneumonia</td>
<td>4</td>
</tr>
<tr>
<td>Atypical pneumonia</td>
<td>2</td>
</tr>
<tr>
<td>Bronchopneumonia and uremia</td>
<td>2</td>
</tr>
<tr>
<td>Congestive heart failure and chronic glomerulonephritis</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure and pneumonia</td>
<td>1</td>
</tr>
<tr>
<td>Toxemia</td>
<td>1</td>
</tr>
<tr>
<td>Hemorrhages</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
</tbody>
</table>

Electrocardiograms were taken in 12 cases. All showed sinus tachycardia. Nine showed some type of abnormality; low voltage was present in 7, T-wave changes in 4, axis deviation in 4, and first degree heart block in 2 cases. Although 9 out of 12 cases had abnormal electrocardiograms no consistent pattern of abnormality was found.

Congestive heart failure with hepatosplenomegaly and edema developed terminally in 3 cases. The shortest duration of the condition from the beginning of the first symptoms to death was five months and the longest six years, with an average duration of two and six-tenths years. As shown in table 2, the cause of death was due to pulmonary complications in 61.1 per cent of the cases.

**Pathologic Data.** In 14 of the 18 cases studied there was an alteration of the connective tissue and muscle fibers in the myocardium. These changes consisted of fine scars, focal fibrinoid metamorphosis of the collagenous fibers which resulted in fragmentation and swelling of these elements, and increased density of the ground substance. There was a mild perivascular infiltration of the lymphocytes and polymorphonuclear leukocytes, and the myocardial fibers were fragmented in some areas. The walls of some small blood vessels showed areas of necrosis of the media, and histiocytic infiltration of the adventitia. The lumen was occluded by hyaline thrombi in some areas. In some cases the only findings were interstitial edema, dense collagen and a few mononuclear cells near the surface. No characteristic Aschoff bodies were seen. Endocardial lesions were present in 8 cases. One of these had subacute bacterial endocarditis of the aortic valve, 1 mitral stenosis and 6 nonbacterial verrucous endocarditis. Figure 1 shows the microscopic findings in the mitral valve of case 8. In this latter case, as seen in the figure, the mitral valve contained many
 verrucous vegetations which formed a continuous line across both anterior and posterior leaflets on the auricular surface just away from the free margin of the valve. The posterior cusp of the aortic valve also contained several small verrucous vegetations but the anterior cusp was spared. The commissures were not fused, and the chordae tendineae appeared normal.

Eleven cases had pericarditis. Five of these had pericardial exudates in the respective amounts of 100, 100, 150, 160 and 300 cc. Of these 11 cases, 6 had acute pericarditis, and 5 had chronic obliterator pericarditis, 2 of which had pericardiomediastinal adhesions. Three cases had hydropericardium in the amounts of 40 (reddish), 550 and 650 cc.

Two cases had left ventricular hypertrophy. Five cases showed a slight degree of coronary atherosclerosis.

Correlation of Clinical and Pathologic Findings. Of the 18 cases, 16 complained of shortness of breath while 14 cases autopsied revealed definite evidence of pathologic change within the heart. Of 4 cases in which chest pain was one of the most outstanding complaints, necropsy revealed acute pericarditis in 1, pleuritis and pericarditis in 2, and lobar pneumonia in 1 case.

In 4 cases which had hypertension there were found some glomerular changes in the kidneys. These changes will be discussed in the section of kidney pathology.

The pathologic cardiac findings in 7 cases with apical systolic murmurs were as follows: Case 12 had a heart weighing 260 Gm. with no deformity of the mitral valve except two pinpoint-sized nodules on its leaflets. Microscopic examination of these nodules revealed coagulation necrosis with infiltration of lymphocytes, macrophages and a few segmented neutrophiles. Case 2 had obliterator pericarditis with normal valves and no cardiac enlargement. Case 9 had a heart weighing 280 Gm. and the myocardium revealed extreme edema, infiltration with oval and round histiocytes, lymphocytes and eosinophils. The valves were normal. Case 16 showed the changes of subacute bacterial endocarditis on the mitral valve. Case 17 had a heart of 300 Gm. and normal valves. In case 18 the heart weighed 230 Gm. The valves were normal and there was some fibrinoid degeneration in the walls of some vessels in the myocardium.

In case 7, in which a late apical diastolic rumble was heard, autopsy disclosed mitral stenosis. In case 10, which had an aortic systolic murmur, autopsy revealed left ventricular hypertrophy and there were fibrinoid necrotic changes in the endocardium of the aortic and mitral valves present on microscopic examination. As shown by the preceding discussion of 7 cases with apical systolic murmurs, only 2 had nonbacterial verrucous endocarditis of the mitral valve leaflets; conversely, of 6 cases with nonbacterial verrucous endocarditis only 2 had an apical systolic murmur.

In 7 cases in which the electrocardiograms showed some kind of abnormality, the postmortem findings were as follows: Case 1, in which the electrocardiogram showed right axis deviation, low voltage and first degree heart block, autopsy revealed pericarditis with 100 cc. of exudates and small scars in the myocardium. In this case the low voltage can be explained by acute pericarditis, and the heart block by focal small scars in the myocardium. Case 2 had a low voltage, elevated RS-T segments in leads I, II, and III with inverted T
waves in leads III and IV. At autopsy, obliterative pericarditis was found. Case 3 had low voltage, and flat T waves in the electrocardiogram. At autopsy acute pericarditis with 100 cc. of exudate in the pericardial cavity was found. Case 4 had low voltage, right axis deviation and first degree heart block. Autopsy revealed obliterator pericarditis and small focal collections of lymphocytes, monocytes and plasma cells in the myocardium. Case 7 had right axis deviation and low voltage of the QRS complexes in the standard extremity leads. Autopsy disclosed 300 cc. of clear, yellow fluid in the pericardial cavity and mitral stenosis. Case 9 had low voltage of the QRS complexes. Necropsy in this case revealed 550 cc. of clear yellow fluid in the pericardial cavity; extreme edema as well as infiltration by oval and round histiocytes, lymphocytes, and eosinophils, were found in the myocardium. Case 11 had left axis deviation, flat T waves in leads I, II and III. At necropsy a chronic pericarditis with petechial hemorrhages, pleuromediastinal adhesions and diffuse petechial hemorrhages in the myocardium were found. Case 15 had low T waves in the standard leads and ventricular premature beats. Autopsy revealed left ventricular hypertrophy, nonbacterial verrucose vegetations on the mitral valve, slight increase in the connective tissue, and numerous small scars in the myocardium. Case 18 had low voltage of the QRS complexes and inverted T waves. At necropsy a pericarditis with 100 cc. of fluid was found.

**Urinary System**

**Clinical Data.** Urinalysis was performed in 17 cases. Of these 17, 14 had abnormal findings. All of these 14 cases at some time while under observation showed albuminuria. One showed albuminuria and slight leukocyturia without other clinical evidence or renal disease; one had albumin, leukocytes and granular casts in the urine. Three cases had albuminuria, cylinduria and hematuria; 2 cases had albuminuria, leukocyturia and hematuria; albumin, leukocytes, erythrocytes and casts were found collectively in the urines of 4 cases. Of 17 cases 3 showed no abnormality in the urinalysis at any time while under observation.

Of the 12 cases in which nonprotein nitrogen determinations were done, 7 showed values in excess of the normal of 40 mg. per 100 cc. of blood. In these cases the premortem clinical diagnosis of chronic glomerulonephritis and uremia was made.

**Pathologic Data.** In each of the 18 cases studied there was some abnormal finding in the kidneys. Thickening of the basement membrane of the capillary loops in the glomeruli with typical “wire-loop” changes was found in 14 cases. Focal necrosis of the loops was present in 2 cases. In 3 cases hyalinization of some glomeruli and scar formations were found. Two cases showed many petechial hemorrhages on the surfaces of the kidneys; one case had numerous pinpoint petechiae throughout the renal cortex; and the other case, hemorrhages into the renal pelvis. One case had chronic glomerulonephritis as well as wire-looping of the glomeruli.

**Correlation of Clinical and Pathologic Findings.** In each of the 14 cases with abnormal urinary findings necropsy disclosed some abnormality in the kidneys. Cases 3, 5, 8, 10 and 15 had albumin, erythrocytes, leukocytes and granular casts in their urine, clinically. In each of these cases, except in case 5, wire-loop changes of the glomeruli were found at autopsy. Case 5 had hyalinization of some glomeruli and scar formation. Cases 11, 14 and 16 had normal urinary findings. Autopsy in case 11 revealed moderate thickening of the glomerular capsule, infiltration with round cells, arteriolar thickening and hemorrhages into the pelvis. Wire-loop changes of the glomeruli and hyaline thrombi in the arterioles were noted in case 14. In case 16 wire-looping of the glomeruli and numerous completely hyalinized glomeruli were found. The hemorrhages into the renal pelvis, seen in case 11, might have occurred terminally and have escaped laboratory recognition in this way. In the latter 2 cases urinary findings were normal in spite of the typical wire-loop changes in the glomeruli. One of these 7 cases had numerous necrotic foci and infiltration of leukocytes into the glomeruli, without wire-loop changes. Of 4 cases which developed high diastolic blood pressures over 90 mm. Hg autopsy revealed wire-loop changes
of the glomeruli in cases 3, 15 and 18, and focal-loop necrosis in case 2. In case 15 in addition to marked wire-looping, some glomeruli were shrunken and tubules showed atrophy and replacement by fibrotic tissue in some areas. Why arterial hypertension is not found consistently in the presence of the kidney pathology is not known.

![Fig. 3. Case 17, onion peel changes in the central arteries of the spleen.](image)

**Gastrointestinal System**

**Clinical Data.** Symptoms and signs referable to the gastrointestinal system were not common. One case had hepatomegaly and splenomegaly of unknown etiology for two years. Nausea and vomiting were outstanding complaints in 3 cases. The liver was enlarged to palpation in 6 of the 18 cases and the spleen was enlarged in 6.

**Pathologic Data.** The pathologic findings in livers of the 18 cases were as follows: 6 cases had slight to moderate degree of fatty degeneration; 1 case had some necrosis of the liver cells; 2 cases had cholelithiasis; 3 cases had some fibrinoid degeneration of the small arteries and perivascular round cell infiltration; and 6 cases had normal livers.

Alteration of the collagen was found in the spleens of 11 cases. In 10 cases the spleen weighed between 120 and 250 Gm., and in 8 cases between 270 and 480 Gm. Hyperplasia of the malpighian bodies, mild arteritis of the small central arteries with intimal proliferation, the hyperplasia of the adventitia resembling "onion skin," perivascular fibrosis and hemorrhages constituted the significant changes found in microscopic examination of the spleens (fig. 3).

Complete tissue necrosis of the pancreas in one and large areas of pancreatic hemorrhages in another case were found.

**Correlation of Clinical and Pathologic Findings.** Of 3 cases which complained of nausea and vomiting, case 18 revealed at autopsy moderate fatty degeneration of the liver and typical onion-peel changes in the spleen; case 5 revealed onion-peel changes in the spleen; and case 4, petechial hemorrhages in the mucosa of the stomach. In other cases in which the gastrointestinal tract showed some alteration of the collagen there were no referable clinical symptoms.

**Respiratory System**

**Clinical Findings.** Dyspnea occurred in 3 cases; chest pain in 5; cough in 6; hemoptysis in 2, and bloody sputum in 1 of the cases. The clinical diagnosis of lobar pneumonia in 5; atypical pneumonia in one; pleurisy in 4; and bronchopneumonia in 3 cases was entertained.

**Pathologic Data.** Sixteen of the 18 cases had some abnormality in the lungs as follows: 7 cases had bronchopneumonia, 1 of which had also atelectasis; 5 cases had lobar pneumonia; 2 cases had atypical interstitial pneumonia and 1 case had atelectasis. Multiple small hemorrhagic areas scattered throughout the right lung were found in 1 case.

Acute pleuritis was present in 3 cases; chronic pleuritis, in 7 cases. In 5 of the chronic cases both pleural cavities were obliterated by many old, fibrinous adhesions. Three cases had bilateral hydrothorax.

**Correlation of Clinical and Pathologic Findings.** The correlation of dyspnea, chest pain and cough with pathologic findings showed that these symptoms were due to either (1) inflammation in the lungs, such as pneumonia or bronchopneumonia or (2) pleuritis or (3) some combination of these conditions. Case
11 gave a history of hemoptysis of four week’s duration and autopsy findings revealed hemorrhages in the subarachnoid space, in the lungs, pleura, pericardium, myocardium, and into the renal pelvis. Case 13, which had bloody sputum, showed at autopsy some atelectasis in the right lower lobe of the lung. Case 16 had cough, dyspnea and hemoptysis and at autopsy bilateral bronchopneumonia was found.

![Image](https://example.com/image.jpg)

**Fig. 4.** Case 7, typical rash of butterfly appearance on the face and erythematous patches on the arm.

**SKIN LESIONS**

Typical rash of butterfly appearance (fig. 4) occurred in 11 cases. Four other cases had some other kind of skin lesions, such as dermatitis on the face in 1 case; seborrheic dermatitis in 1 case; and nonspecific erythematous lesions on the trunk in 2 other cases. Of the 15 cases with some kind of skin lesion, joint pains preceded the skin manifestations by 5, 11 and 12 months in 3 such cases.

**COMMENT AND SUMMARY**

In a study of the clinical and pathologic findings in 18 cases of acute and subacute disseminated lupus erythematosus confirmed at necropsy it has been observed that this disease is more common among females, between the ages of 22 and 33, than males. This is in complete accord with previous observations.

Joint pain was the most common symptom, being encountered in 72.2 per cent of the cases studied.

A rash of butterfly appearance was encountered in 61.1 per cent of the cases. Four other cases had some kind of nonspecific skin lesions. Joint pains preceded skin lesions in only 3 cases, and in others they were either coincident with skin manifestations or occurred some time after them. Two other cases had joint pains for several months but they never had any skin manifestation and autopsy performed in these cases disclosed no lesions of rheumatic fever. This study shows that polyarthralgia due to acute and subacute disseminated lupus erythematosus may occur without any skin manifestation of the disease. In any polyarthralgia with an unknown etiology acute disseminated lupus erythematosus should be considered, although the occurrence of it without skin lesions is not frequent.

The involvement of the heart is very common. In 14 of the 18 cases studied there was an alteration of the connective tissue and muscle fibers in the myocardium. However, there was no constant correlation between clinical findings and specific pathologic lesions found in the heart. Neither murmurs heard over the precordium nor QRS and T-wave changes seen in the electrocardiogram were pathognomonic for the disease. A systolic murmur heard at the mitral area in a patient with disseminated lupus erythematosus might suggest the involvement of the endocardium, but, according to this study, this is usually not the case. Of 7 cases with apical systolic murmurs only 2 had nonbacterial verrucose endocarditis of the mitral valve leaflets; conversely, of 6 cases with nonbacterial verrucose endocarditis only 2 had an apical systolic murmur. Electrocardiographic changes are of clinical significance in that they suggest pericardial or myocardial involvement. Low voltage, elevated RS-T segments, inverted T waves, prolonged P-R interval are indicative of changes in pericardium or in the myocardium, but are not specific for the disease itself.
In the cases studied the most common laboratory finding was albuminuria, this being found in 82.3 per cent of the patients. There was no constant correlation between clinical and specific pathologic findings. The commonly encountered wire-loop changes of the glomeruli may cause albuminuria, leukocyturia, cylindruria, high nonprotein nitrogen of the blood, and hypertension collectively, or one of these signs separately, or there may be no clinical findings.

In the presence of a typical butterfly rash the diagnosis of lupus erythematosus is not difficult, but in 39 per cent of these cases the butterfly rash did not occur. In the absence of the typical skin manifestation, the findings which were most constant and suggestive of the disease were as follows: (1) polyarthralgia of undetermined origin, (2) fever and tachycardia of unknown cause, (3) albuminuria alone, or together with hematuria, and cylindruria, (4) leukopenia, and (5) signs and symptoms of serosal inflammation.

Therefore the diagnosis of disseminated lupus erythematosus should be suspected when a female in the early decades of life presents herself with shortness of breath, a skin rash, multiple joint pains, fever and tachycardia, and in whom there is found evidence of pulmonary, cardiac and kidney abnormality. The diagnosis is confirmed by biopsy of the skin lesion, the finding of an anemia and leukopenia, a high globulin content in the serum (above 2.5 Gm. per 100 cc.) and the detection of typical lupus erythematosus cells in the peripheral blood or in the bone marrow.

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