SYSTEMIC LUPUS ERYTHEMATOSUS

Description of 37 Cases in Children and a Discussion of Endocrine Therapy in 32 of the Cases

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Systemic lupus erythematosus in children is generally a progressive disease terminating fatally. With the advent of adrenocorticotropic and adrenal steroid hormones and subsequent reports1-3 of successful treatment in adults, it seemed possible that the prognosis in children might also be improved. This paper presents a detailed description of clinical and pathologic features of systemic lupus erythematosus in 37 children, 32 of whom were treated with adrenal steroids or adrenocorticotropin.

CASE MATERIAL

The 37 cases described include all those children under the age of 14 years seen at the Children's Hospital (Boston) between 1916 and 1959 and at the Babies and Children's Hospital (Cleveland) between 1953 and 1959, in whom the diagnosis of systemic lupus erythematosus could be substantiated by the clinical, laboratory or pathologic findings.

CLINICAL FINDINGS

General Features

The disease is one affecting many organ systems, and the patients presented with a wide variety of clinical manifestations. No single symptom or sign was considered diagnostic, but, as the disease progressed, involvement of skin, joints, kidneys and blood-forming organs resulted in the classic syndrome in most instances. Since 1948, the L.E. cell phenomenon has proven very reliable for diagnosis.

Six atypical cases without facial rash have been included on the basis of characteristic laboratory or pathologic findings.

All but 3 of the 37 children in whom the diagnosis of systemic lupus erythematosus was made were girls, and, with the exception of 7 cases, the disease became manifest between the ages of 9 and 13 years (Fig. 1). Twenty-seven of the children were followed until death. Of the remaining 10 children, 8 have survived for 2 or more years. In the fatal cases the duration of the disease from the earliest sign or symptom ranged from 8 weeks to 5 3/12 years.

The children came from a widely varied racial (including two Negroes) and socioeconomic background. The family history was significant in five children. Two girls each had a sister who also died of systemic lupus erythematosus, and the father of another child had discoid lupus without any systemic involvement. Two other children each had a sibling with rheumatoid arthritis.

Possible Precipitating Factors

The identification of precipitating factors in the disease was complicated by the frequent occurrence of nonspecific prodromal symptoms which included intermittent fever, malaise or arthralgia. In 22 children no precipitating factor could be ascertained.

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and in none of the others could any definite causal mechanism be determined. However, in seven cases severe sore throats (one proven streptococcal) preceded the onset of the disease by 2 to 4 weeks. One child had an initial mild respiratory infection, another a preceding abscessed tooth. In one child the onset of the disease and two subsequent exacerbations were closely associated with the menses. Exposure to the sun coincided with the onset of the initial sign, an erythematous facial rash, in two children. Four children came from disturbed homes, and the initial symptoms followed closely upon episodes of severe psychologic stress.

**Initial Symptoms**

In 45% of the children with skin manifestations, the rash appeared in March and April (Fig. 2). The onset of the disease itself showed no such striking seasonal incidence, although a slightly greater number of cases began during the first 6 months of the year.

An erythematous rash was the only symptom in four patients for several months before systemic disease became apparent. In another 15 patients the initial complaint consisted of an erythematous rash of butterfly distribution, but this was accompanied by moderate to high spiking fever, general malaise and arthralgia (Fig. 3). In contrast to dermatomyositis, where arthralgia is rarely present, that was a frequent initial symptom and occasionally was accompanied by objective evidence of involvement of the joints. Twelve patients originally had intermittent arthralgia with or without fever for variable periods ranging up to 3 years prior to the appearance of any facial rash. This arthralgia had been variously diagnosed as rheumatic fever, rheumatoid arthritis or chronic infection. Thrombocytopenic purpura was one of the first manifestations of the disease in four children, in one of whom this symptom occurred 3 years before the appearance of other signs of systemic lupus erythematosus. In five children signs and symptoms of renal disease were the primary reasons for hospitalization. In an additional two patients car-
dial failure was the basis for the presenting complaint. Hemolytic anemia was the initial finding in one patient.

Fifteen patients were seriously ill within 6 months after their first symptoms appeared. The onset was acute and fulminant in five patients who were hospitalized within 1 month and died within 2 to 6 months of first becoming ill. One child had a severe sore throat for 4 weeks followed by the ap-
pearance of a butterfly type of rash. This rapidly spread to involve the entire face, neck and upper arms, and was soon associated with sore mouth, epistaxis, migratory joint pains, high fever, frequency and dysuria. Death occurred only 6 weeks after the appearance of the rash. In another child the butterfly type of rash and joint pains, malaise and fever appeared simultaneously; the course was rapid, terminating with interstitial pneumonia within 8 weeks.

**Skin**

The facial rash, when present, was strikingly erythematous, covered the malar areas and extended over the bridge of the nose in most cases. While involvement of the lower lids occurred, the upper lid was usually spared, and the heliotrope discoloration of the upper eyelids and periorbital edema so characteristic of dermatomyositis were not seen in these children. Late in the course of the disease the facial lesions occasionally became vesicular and bullous, and the skin and subcutaneous tissue necrotic and secondarily infected. As the disease progressed, the rash, which was at times hemorrhagic, often extended to involve the entire face, scalp, neck, chest and upper arms (Fig. 4). Occasionally this rash became morbilliform or might simulate a rash of drug sensitivity. Vesicular skin lesions, which corresponded to the eruption of herpes zoster in character and distribution, were observed in three patients.

Erythematous macular lesions of the hands, finger tips and feet were found in almost half the children and were the initial complaint in one child. These lesions were often intensely pruritic. Faintly erythematous lesions with prominent tiny vessels over the extensor surfaces of the joints, somewhat analogous to the lesions seen in dermatomyositis, were occasionally seen in these patients. Several of the children showed changes in the fingernail beds which varied from thromboses and tortuosity of the capillaries to subungual hemorrhages, marked

![Fig. 4. Left, Facial lesion. This rash was markedly erythematous and, Right, extended to include other parts of the body.](http://pediatrics.aappublications.org/)
inflammation of the cuticle and a definite tendency to paronychiae.

Thirteen of the children had petechiae, usually associated with thrombocytopenia. Thromboembolic phenomena involving the fingertips and leading to actual tissue necrosis were also noted in several of the patients.

Exacerbation of the rash on exposure to sunlight was noted in nine children. However, the classic relationship between exposure to the sun and exacerbation of systemic manifestations of the disease was noted in only two cases. This may have been the result of cautioning the patients against such exposure. In addition, the fact the rash began most frequently in the winter and spring months rather than the summer months (Fig. 2) at least suggests that actinic sensitization is not an important causative factor.

Partial alopecia was found in approximately one-fourth of the children. In the patients surviving an additional few months after the appearance of this finding, the hair often returned to a normal appearance.

Mucous Membranes

Lesions in the mouth consisted most typically of gingivitis and hemorrhages in the gums, but often included punctate or ulcerating lesions of the buccal or palatal mucosa; these were seen in approximately half of the children. Marked vulvo-vaginal inflammation was noted several times.

Kidneys

The phase of systemic lupus erythematosus which proved most serious was the renal involvement found in 33 of the patients; it was the primary or one of the important contributory causes of death in 18. In five children pyelonephritis complicated the classic nephritic picture. The clinical manifestations of renal involvement consisted of edema and moderate to marked hypertension in approximately half of the patients. In addition, renal failure undoubtedly played a role in the pericarditis, neurologic disturbances, bleeding tendency and anemia seen in the later stages of the disease in a number of patients.

Reticuloendothelial System

Enlargement of the liver was noted at some time during the course of illness in 15 of the patients and significant splenomegaly was noted in 16. Generalized lymphadenopathy was never a prominent finding.

Heart and Lungs

Cardiac abnormalities, including significant systolic murmurs, cardiac enlargement or the presence of a gallop rhythm, were observed in 20 of the patients. Cardiac failure was an important contributory factor in the death of two patients. Three children had clinical evidence of pericarditis in the absence of uremia. Pleural effusions and pneumonia were relatively frequent complications.

Neuromuscular Systems

Complications occurred in the central nervous system in a third of the patients. Most frequently these consisted of convulsions, in some cases secondary to uremia and hypertension, but in others presumably representing primary involvement of cerebral vasculature. Two children developed hemiplegia and three others exhibited extensive muscle weakness, in excess of that expected in the primary disease itself. Although this weakness occurred while receiving steroid therapy, the dosage was small in each instance.

Funduscopic examination showed cytoid bodies in only one patient. In this child the characteristic lesion regressed and finally disappeared in spite of progression of the general disease.

Other Manifestations

Prior to the era of effective antibacterial therapy, infection was a serious threat to survival of children with systemic lupus erythematosus. Infection was the direct cause of death in three of the cases; one died of Clostridium welchii peritonitis, the
other two of bronchopneumonia. One child had an extensive infection of the facial lesion. Non-fatal staphylococcal sepsis occurred in two children; generalized moniliasis was a terminal complication in one case following 5 months of penicillin therapy; and one patient was found at necropsy to have torulosis. Two of the children had unexplained swelling and tenderness of the parotid glands during the height of the systemic disease. Two patients had necrotic perforations of the nasal septa.

Several children had persistently positive guaiac tests of their stools during the last months of illness. Terminal episodes of hemorrhage occurred in five of the patients, the principal sites being cerebral, pulmonary, nasal, gastrointestinal, vaginal and cutaneous.

Six of the children presented serious problems in cross-matching of blood and some of these experienced severe transfusion reactions, even with the most carefully matched blood. In two patients, these reactions contributed to terminal renal failure.

LABORATORY FINDINGS

Blood

Examination of the blood revealed few diagnostic features except for a positive L.E. cell preparation in 31 of the 32 cases in which this test was performed (Fig. 6). Originally, bone marrow preparations were used, but the characteristic L.E. cell (Fig. 6) is more easily demonstrated in the buffy coat of minimally heparinized venous or capillary blood. Early in the course of the disease, the L.E. cell phenomenon could be suppressed by massive steroid therapy, although terminally these compounds exerted no apparent effect. Out of approximately 300 patients tested for the possibility of systemic lupus erythematosus, only one apparently false-positive L.E. cell preparation was encountered and that one was in an adult.

Examination of the blood at the time of admission characteristically showed a normochromic, normocytic anemia of variable severity and a normal reticulocyte count. During the course of disease, the hemoglobin level declined to below 10 gm/100 ml in three-fourths of the patients, while 20% developed severe anemia (hemoglobin less than 6 gm/100 ml). In a number of these latter cases there was an obvious hemolytic component, while in others the presence of a positive Coombs’ test or hemagglutination suggested hemolysis as a contributing factor. Leukopenia (less than 5,000 leukocytes/mm³) was present early in the disease in 13 cases and at some time in the course of the disease in 21 cases. Leukocytic response to infection often was decreased, but in some cases was normal. Occasional myelocytes, frequent band forms, and polymorphonuclear cells with toxic granulations were observed. Granulocytopenia was seen only once.
Six patients had thrombocytopenia. One child presented with a diagnosis of idiopathic thrombocytopenia which was alleviated by splenectomy. She remained well for 9 months, only to return with symptoms of systemic lupus erythematosus. However, the thrombocytopenia did not recur despite severe manifestations of the disease. Terminally five children had serious hemorrhages which were considered to be due to deficiency of platelets.

Bone marrow specimens most frequently appeared normal, although 3 of 8 specimens were hypocellular, with mild depression of the erythroid series in 2 and of the myeloid cells in 1.

Biologically false-positive serologic tests for syphilis were seen in 6 of 29 cases tested. In 2 of 20 patients tested, the antistreptolysin titer was elevated. The heterophile test and agglutination tests for febrile diseases were negative when done. The erythrocyte sedimentation rate was elevated in 29 of 31 cases. The latex-fixation test for rheumatoid arthritis was negative in eight cases tested.

In those patients who improved after administration of cortisone or adrenocorticotropin, an early laboratory finding was an increase in reticulocytes up to 10% with a subsequent elevation of hemoglobin. Inconstantly, a low leukocyte count was also seen to increase, with a preponderance of young myeloid cells.

**Plasma Proteins**

These were measured in 21 of the children. The total proteins were within normal limits, but in three cases the albumin:globulin ratio was reversed. Electrophoretic studies of the serum of a number of the patients showed an increase in alpha2- and a marked increase in gamma-globulins.
Renal Studies

All but 4 of the 37 children showed definite evidence of renal involvement at some time during the course of the disease. The earliest indications were: a slight increase in 24-hour urinary excretion of protein and microscopic hematuria; leukocyturia; and decreased clearances. Ultimately renal failure ensued in approximately two-thirds of the patients. This was characterized by edema, hypertension, azotemia, acidosis, electrolyte imbalance and terminal convulsions. In most instances the inexorable progression of the nephritic manifestations appeared unaffected by therapy, but in 6 of the 10 surviving patients definitely abnormal urinary findings reverted to or toward normal concomitant with the administration of large doses of adrenocorticosteroids. Addis counts of the urinary sediment were often employed to follow the course of renal involvement.

Additional findings consistent with pyelonephritis were present in five cases.

Roentgenograms

Roentgenograms of the chest were useful in defining cardiomegaly, pleural effusion and pneumonia.

Electrocardiograms

Abnormalities were observed in the tracings from 19 cases. The primary changes were depression of the T waves with prolongation of A-V conduction in some cases; these disturbances were interpreted as evidence of myocarditis.

Liver Function Tests

In 20 of 22 children cephalin-cholesterol flocculation, thymol turbidity and thymol flocculation tests were positive, usually strongly so; these are indicative of changes in gamma-globulin in the serum, presumably related to liver function. Neither direct nor indirect bilirubin was more than minimally elevated in the plasma, except when hemolysis had occurred.

Intradermal Leukocyte Test

All five patients tested with intradermal injections of either homologous or heterologous leukocyte suspensions developed a delayed hypersensitivity reaction consisting of redness and edema appearing after 24 to 48 hours, although in one child this test remained negative until after steroid therapy had been temporarily discontinued.

Miscellaneous Tests

The tuberculin skin test was positive in two cases and negative in all the others. Lumbar puncture was performed in four cases, and the cerebrospinal fluid was within normal limits in all.

PATHOLOGIC FINDINGS

General Features

In 14 of the 27 children who died, necropsies were either performed at the Children's Hospital or the histologic slides and gross necropsy findings were reviewed by one of us (J.M.C.). In all but one of these (a child who had characteristic clinical findings of lupus, but died of sepsis) there was adequate gross and microscopic evidence to establish a diagnosis of systemic lupus erythematosus. The important pathologic diagnostic criteria were: wire loop lesions of the renal glomeruli, nonbacterial verrucous endocarditis (Libman-Sacks), or a typical lupus skin lesion—all in association with fibrinoid necrosis of the connective tissue (Fig. 7). Hematoxylin bodies were identified in most of the cases. The bodies of six of the children were wasted at necropsy and another six showed peripheral edema. Macular, erythematous or petechial rashes were present in all instances. In nine of the cases the facial skin lesions of a typical butterfly distribution were evident after death.

Vascular Lesions

Although not by itself diagnostic, the single most consistent and wide-spread pathologic finding was arteritis. We are indebted to Donald Brown, M.D., formerly of the Beverly Hospital, to Dr. Lester M. Friedland, of the Holyoke Hospital, and to Dr. Gustav Dammin, of the Peter Bent Brigham Hospital, for permission to use the necropsy material from three of the cases.
finding was the change in the arteries and arterioles, which consisted of hyaline fibrinoid necrosis of the media, proliferation and swelling of the intima, and a varying degree of periarterial inflammation (Fig. 8). These changes in the coronary vessels were occasionally associated with acute myocardial damage; in the gastrointestinal tract there were secondary areas of erosion, particularly in the esophagus and small intestine. In the liver, spleen and pancreas the vascular lesions led to secondary infarction and thrombotic occlusive arteritis. The arteries of the lungs also showed characteristic hyaline necrosis. Arteriolar degeneration was found in vessels in the adrenals and the pelvic viscera and in the vasculature of the muscles. Similar perivascular inflammatory cuffs were noted in the arteries of the central nervous system. The most important alteration in the kidneys was also related to vascular changes and will be described in detail.

**Renal Lesions**

In all cases the kidneys showed some degree of glomerular or acute arteriolar involvement. In eight cases the kidneys were overweight by at least 25%, and in 2 by 100%. Gross petechial hemorrhages were observed in eight cases, al-

![Fig. 8. Spleen, showing typical periarterial swelling of the reticulum and fibrosis. (Toluidine blue and eosin, ×600.)](image-url)
though no kidney had gone on to gross scarring with adherence of the capsule. The glomeruli were significantly damaged microscopically in 12 cases, 8 of them showing the characteristic wire loop lesions of the tuft (Fig. 9). Other glomerular changes included capsular proliferation (8 cases), fibrin plugging of the capillaries (8 cases), endothelial swelling and proliferation (6 cases), collagenous thickening of the tuft (6 cases), and glomerular scarring, though periglomerular scars were found in others. Active tubular degeneration was found in six cases, and evidence of tubular atrophy in three. Arteriolar damage was present in nine instances and was characterized by endothelial cell swelling and proliferation, which was most often the predominant change. Proliferative, hyaline and fatty changes in the media were occasionally present, but did not dominate the picture. Obliterative periarteritic degenerative lesions of the large muscular arteries were present in four cases; these were often occlusive and gave rise to areas of infarction in two cases. Interstitial inflammation was present in six instances to a degree more severe than could be accounted for by the glomerular and arterial damage already noted. Taken by themselves, the kidneys in four patients showed features more characteristic of subacute glomerulonephritis; in two of these periarterial lesions were important components, while in a third case prominent periarterial involvement of the larger vessels was associated with very typical lesions of systemic lupus erythematosus in the remainder of the kidney. In four cases the lesions of the kidney were considered to be of minor clinical significance.

Serous Effusions

These were present in 10 cases, occurring with equal frequency in the pericardial, pleural and abdominal spaces. Ascitic fluid was usually greatest in amount and ranged up to 2,500 ml. Fibri nous or obliterator serositis was present in seven cases, the same type and stage of reaction being noted in all affected cavities. In one instance the ascitic fluid was blood-tinted; in this there was rather marked involvement of the larger arteries with a periarteritic reaction.

Heart and Lungs

Cardiac enlargement was very common; in nine cases the heart was at least twice the normal weight for the age. However, thickening of the individual chambers was significant in only three, all of which showed left ventricular hypertrophy. Marked dilation was present in the right chamber in only a single case, and here the causative factor was not obvious. Valvular lesions (Fig. 10) of the Libman-Sacks variety were present in seven cases, the mitral valve being involved in all seven and the aortic,
Reticuloendothelial System

The spleen was enlarged to twice its normal weight in one-third of the cases. The characteristic vascular change (Fig. 8) was present in 11 cases, and further swelling and proliferation of reticulum fibers about the perihilar arteries was present in six of these. The red and white pulp were depleted of lymphocytes in all instances, but in four the white pulp and/or the connective tissue were infiltrated with polymorphonuclear cells. Plasma cells in increased numbers were present in the red pulp in three cases, and active phagocytosis of leukocytes was noted in one.

The liver was overweight by 200 or more grams in half the cases, though this enlargement could be ascribed to congestion in only two. In 5 of the 14 cases foci of necrosis secondary to vascular changes were present in the liver.

Though the appearance of the lymph nodes probably more often reflected a response to changes in the field of drainage rather than general reactive changes in the body, three pathologic features were seen frequently enough to warrant mention. These included hyperplasia and swelling of the sinusoidal reticulum cells in four cases, hyperplasia and prominence of the plasma and pre-plasma cells in eight instances, and lastly, swelling and prominence of the reticulum fibers in the node in five.

The total cellularity of the bone marrow at postmortem examination was more often hypoplastic than hyperplastic; in five cases a significant decrease in total cellularity was found. This decrease in cells predominantly affected the myeloid series, since a relative increase in erythroid forms was found in five cases. In only two cases were the erythroid series believed to be relatively depressed in relation to the number of myeloid forms. An increase in plasma cell forms was noted in the marrow in five instances, so that in 10 of 14 cases plasma cell hyperplasia was found in either lymph nodes, spleen or bone marrow. Marked activity of the phagocytic cells of the marrow toward erythrocytes was noted in five instances.

Gastrointestinal Tract

The gastrointestinal tract showed areas of erosion secondary to vascular changes. The esophagus and small intestine were most often

Fig. 10. Characteristic verrucal excrescences on heart valve. The right ventricle has been opened and the tricuspid valve has been reflected upward.
involved (six cases) in such a process, although the stomach and large bowel were almost as frequently affected. In two instances large arteries had the typical changes of periarteritis nodosa and in one of these there was a resulting duodenal perforation due to ischemia of the intestinal wall.

**Skin**

The microscopic sections often did not reflect the true status of the skin as seen during life, or grossly at necropsy, since restrictions did not allow removal of lesions of the face or neck. However, in the sections obtained, keratin plugging of the hair follicles was found in eight cases, a mild inflammatory reaction in four and a more severe one in four, with atrophy present in six cases. Edema was noted in two and hyaline connective tissue changes in a single case only.

**Skeleton**

No significant lesions of the bony structures were found.

**THERAPY**

It is apparent from the high mortality in this series of children that there was and is no specific, consistently curative therapy for systemic lupus erythematosus. However, certain agents provide symptomatic benefit and occasionally seem to induce prolonged arrest of the underlying process.

As can be seen in Table I, various therapeutic regimens have been used. Treatment aimed at the possible pathogenesis of the disease has been limited to attempts to alter the formation of antibody, or to interfere with its interaction with a hypothetical antigen. In this category are gold salts and bismuth, which had no effect in two children. Radiation and nitrogen mustards prevent the development of antibodies and lesions of hypersensitivity in experimental animals, when given prior to the injection of antigen in doses which depress the leukocyte count.\(^6\) Spray radiation did produce temporary symptomatic improvement in one patient, but was of no benefit in another child. Nitrogen mustards were used in three patients; two of these girls exhibited partial remission lasting 2 and 4 months with virtual disappearance of the facial rashes, fever and generalized symptoms and a decrease in the urinary findings; the third child received the drug only terminally and showed no benefit. The administration of nitrogen mustards was associated with severe reactions, characterized by nausea, vomiting, prostration and an extreme leukopenia (less than 100 leukocytes/mm\(^3\)).

Adrenocorticotropic and adrenocorticosteroids, used singly or in combination, are believed to affect hypersensitivity disease by diminishing the formation of antibodies or by reducing the inflammatory reaction that may result from a possible antibody-antigen reaction. These agents were used in 32 of the patients. In the first patients treated it was found that, in spite of attempts to reduce the dose of corticosteroids gradually, there was shortly a recrudescence of the disease. Because of this, and because of the failure to influence the outcome with therapy directed only at symptomatic control, recent patients have been given (even when symptom-free) as large doses of corticosteroids as they could tolerate without evidence of serious toxicity, such as dangerous hypertension or marked fluid or electrolyte imbalance. Although

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**TABLE I**

<table>
<thead>
<tr>
<th>AGENTS WHICH HAVE BEEN SUGGESTED FOR THERAPY OF SYSTEMIC LUPUS ERYTHEMATOSIS</th>
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</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
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<tr>
<td>Bismuth</td>
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<td>Gold salts</td>
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<tr>
<td>Radiation</td>
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<tr>
<td>Nitrogen mustards</td>
</tr>
<tr>
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<tr>
<td>Injections of leukocytes*</td>
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<td><strong>Supportive</strong></td>
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<td>Transfusions</td>
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<td>Antibiotics</td>
</tr>
<tr>
<td>Digitalis</td>
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<td>Splenectomy</td>
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* Currently being used or under investigation.
LUPUS ERYTHEMATOSUS

some patients with advanced renal disease and hypertension may not tolerate such therapy, on the basis of our experience with seven patients treated with large doses for prolonged periods of time it would appear that the disease process may be made to regress and to become quiescent.

Therapy of systemic lupus erythematosus is difficult to evaluate because of the extremely variable course of the disease: 56% of the children with this disease die within 2 years of the onset (Fig. 1) but some children may survive as long as 4 or 5 years and still succumb; such children are usually older at the time of onset.

At the time of this report, five patients are considered to be in remission. Two of these have discontinued corticosteroid therapy without evidence of recrudescence for 8 months and 4½ years, respectively. All five were in the older age group and would thus perhaps be expected to survive for a more prolonged period. Nevertheless, the striking association of corticosteroid administration with complete remission of symptoms and the actual reversal of abnormal urinary findings in 6 of 10 surviving patients at least suggests that administration of these agents is a potentially effective therapeutic measure. Remissions of this nature have not been encountered by the authors in untreated or partially treated patients, but conversely it must be stressed that in some the renal disease progresses in spite of vigorous steroid therapy.

Since the extent and reversibility of the renal lesion usually determines the survival of the patient, it is particularly important to treat the child with minimal or even absent renal involvement in the hope of preventing renal damage. Because of the high mortality of children with systemic lupus erythematosus, therapy with steroids appears justified in spite of its many and sometimes fatal side effects.7

The fact that systemic lupus erythematosus occurs so predominantly in females provides a tenuous theoretic basis for the use of testosterone. Testosterone propionate Linguets* were used in three cases in an unsuccessful attempt to maintain remissions induced by adrenocorticotropin or cortisone.

Currently attempts are being made to evaluate the therapy suggested by Kurnick8 using intramuscular injections of leukocytes, but it is too soon to evaluate this form of treatment. In addition, chloroquine9 has been used in five patients, but with only equivocal results to date. Details of current therapy are given in Table II.

Treatment of secondary complications of systemic lupus erythematosus is important. Occasionally infections are present and should be eradicated if possible by the appropriate antimicrobial agents. Anemia should be corrected with transfusions only when severe, as serious transfusion reactions may occur.

DISCUSSION

On the basis of this analysis of the clinical, laboratory, and pathologic data from 37 cases of systemic lupus erythematosus under 14 years of age, it is apparent that this is an extremely serious disease with a very poor prognosis. These findings are consistent with reports of others.10,11 The disease is protean in its manifestations, affecting the cardiovascular system, the central nervous system, the lungs, the liver, the skin, the bone marrow, the joints, but most importantly the kidneys.

This disease may present in a wide variety of ways; e.g., as intermittent fever, arthralgia, thrombocytopenia, progressive renal disease, or as cardiac failure. The characteristic facial rash may be present only late in the disease or in some cases not at all. The introduction of the L.E.-cell test has facilitated the diagnosis but the L.E.-cell phenomenon may be suppressed by steroid therapy.

The disease is much more common in girls but may occur in either sex. Although systemic lupus erythematosus in adults is

* Testosterone propionate Linguets were supplied by Ciba Pharmaceutical Products, Inc., Summit, New Jersey.
# TABLE II

**Therapy of the 10 Surviving Patients**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age at Onset (yr)</th>
<th>Date of Onset (mo, yr)</th>
<th>Renal Involvement</th>
<th>Duration Before Onset of Therapy (yr)</th>
<th>Duration of Disease to 1-1-60 (yr)</th>
<th>Prednisolone* (mg/day)</th>
<th>Leukocyte Injections</th>
<th>Duration of Chloroquine Therapy to 1-1-60 (yr)</th>
<th>Chloroquine (mg/day)</th>
<th>Still Being Treated</th>
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* Prednisolone or an equivalent dosage of another steroid.
** Prior to diagnosis of disseminated lupus erythematosus; since diagnosis leukocyte injections have been used.
† All of these patients have developed the features of Cushing's syndrome and in some cases, hypertension.
similar to that encountered in children, the two age groups differ in one important respect, namely, in severity. The mortality reported for adults has not been as high as the present series would suggest for children, and adults have responded favorably to steroid therapy more frequently.

In our experience, adrenocorticotropin or adrenal corticosteroid therapy has been of definite symptomatic benefit; in six cases prolonged treatment has been associated with disappearance of urinary abnormalities. At the present time, we believe that all children in whom the diagnosis of systemic lupus erythematosus can be definitely established (and especially those in the early stages of the disease) should be treated vigorously with adrenal corticosteroids for a long period of time, probably in most cases for more than 1 or 2 years. However, even with such therapy relentless progression of the disease will frequently occur.

The findings from necropsies of 14 cases of systemic lupus erythematosus from this series showed that all of the children had renal involvement with either typical glomerular lesions or arteriolitis or both. Two of these had negative urinalyses, although it is possible that if Addis counts of the urinary sediment had been done, the early stages of renal involvement might have been detected during life. Obviously, the renal lesion in this condition is most often the critical factor in determining survival. In addition, it is apparent that the efficacy of any therapeutic regimen can be best determined by following renal function or renal morphology. Arteriolar involvement throughout the body was also seen frequently, as was cardiac enlargement and verrucal endocarditis. When the cardiac involvement is severe enough, cardiac failure may contribute to death.

These children are prone to infection, but since the advent of antibiotics none have succumbed to this complication. However, terminal pneumonia (superimposed on cardiac and renal failure) was frequently found to be present at necropsy.

SUMMARY

An analysis of 37 cases of systemic lupus erythematosus in children is reported in order to demonstrate the course of this disease and its pathology. In this series 92% of the children were girls.

Necropsies of 14 cases of the present series revealed characteristic renal findings in all, even when clinical evidence of renal disease had been absent. Generalized arteriolitis as well as evidence of cardiac involvement was usually present. Renal failure was the most frequent cause of death.

Of the 37 children, 10 were alive at the time of this report; 8 of these surviving patients have been followed for more than 2 years. Steroid therapy was associated with partial or complete disappearance of urinary abnormalities in six children. Endocrine therapy was used in 32 of the children with symptomatic improvement in most cases.

Until more specific drugs are available, an intensive and prolonged course of therapy with adrenal corticosteroids offers the best, though limited, chance of slowing or halting this disease process.

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DIABETES, Robert H. Williams, M.D., editor, New York, Paul B. Hoeber, 1960, 793 pp., $20.00.

Each chapter in this book is an essay by one or more of the 54 authors. The expected overlapping and repetitions and the uneven quality make reading very frustrating at the same time that it can be very rewarding. Some of the chapters on the basic alterations in physiology in diabetes mellitus are among the best and certainly the most concise and clear reviews that this reviewer has ever read. But the discussion of the clinical management of children with this disease was disappointing.

The material on therapy of patients with diabetes mellitus is less helpful than the considerations of the basic alterations in physiology. The editor states that an attempt was made to avoid discussion of controversial subjects. This fact, coupled with the apparent difficulty in presenting principles of therapy unencumbered by ritualistic dogmatism, might have made it preferable to have omitted most of the discussion of therapy. From the excellent material in this book, a truly superior and readable volume could have been achieved. I assume that the eminence of the authorities made proper editing next to impossible. It is still a valuable book for the selective reader.

ROBERT KLEIN, M.D.
SYSTEMIC LUPUS ERYTHEMATOSUS: Description of 37 Cases in Children and a Discussion of Endocrine Therapy in 32 of the Cases
Charles D. Cook, Ralph J. P. Wedgwood, John M. Craig, John R. Hartmann and Charles A. Janeway

*Pediatrics* 1960;26;570

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