THE CLINICOPATHOLOGICAL PRESENTATION OF CONNECTIVE TISSUE DISEASES AT KENYATTA NATIONAL HOSPITAL.

A PROSPECTIVE STUDY: 1985 - 1986

BY

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D E C L A R A T I O N

This thesis is my original work, and has not been presented for a degree in any other University.

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This thesis has been submitted for the degree of Master of Medicine with my approval as a University Supervisor.

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Abbreviations

A.N.A.	-	Antinuclear antibody
C.T.D.	-	Connective tissue disease
LE	-	Lupus erythematosus
LE cell	-	Lupus erythematosus.
ECG	-	Electrocardiogram
EMG	-	Electromyograph
DMS	-	Dermatomyositis
R.A.	-	Rheumatoid Arthritis.

SUMMARY

In a prospective study of Connective Tissue Diseases presenting at Kenyatta National Hospital within a period of one year (1985 - 1986), there were 20 patients seen with systemic lupus erythematosus, 10 with systemic sclerosis 3 with morphea and 3 with Dermatomyositis and 11 with Discoid Lupus. Their clinical presentation did not differ from that described elsewhere. Antinuclear antibodies were found in 100% of systemic lupus erythematosus patients, 23.1% of scleroderma, 16.6% of Rheumatoid arthritis, 1 patient with Dermatomyositis and in 3.5% of the controls but not in the Discoid lupus patients. Serum complement levels, immune complexes and immunoglobulins were also found to be abnormal in some of the patients and where they were abnormal they were found to correlate well with disease activity and in some cases to be of a predictive value in the course of the disease.

INTRODUCTION

The Collagen system and the Connective Tissue Diseases.

A System is a group of structures composed of similar elements which combine to perform the same general function. The connective tissue can be regarded as a system as it consists of an association of similar cellular and fibrilla elements held together by an amorphous ground substance of a colloidal nature and it is found throughout the body.

Collagen is the major component of connective tissue and forms the major fibrous component of tendons, ligaments blood vessels and 75%[1] of the dermis which contributes 15 - 20% of the body dry weight.

Originally the disorders attributed to this system were thought to be due to disturbances within the collagen fibres and ground substance and were appropriately known as collagen tissue diseases, but with the subsequent recognition of the importance of the role of other cells, they were renamed connective tissue disease.

A Review of the history of connective tissue disorders.

The interest in arthritis and related disorders goes back to the 18th century. It was during this period that Boerhaave in 1721 and Cullen in 1781,

described the clinical features of rheumatic fever and Curzio in 1754 described systemic sclerosis. It was also around this time that pathology was established as a science and clinico-pathological correllations were becoming an established practice, that Morgagni did a classical study on connective tissue diseases and rheumatoid disease.

A century later people began to look at the concept of disease as involving systems. Cazenave[1] in 1850 described Discoid lupus as it involved the skin, followed in 1872 by Kaposi [1] who described the systemic form, bringing to light the visceral involvement. In 1859 Garrod[1] recognised the different forms of arthritis and introduced the term rheumatoid arthritis to describe the clear out clinical entity. The last of these diseases to be described was Dermatomyositis in 1883 by Wagner.

Towards the end of the 19th century when bacteriology was at its height, scientists failed to find evidence of these diseases being infective in nature and it was not until early this century that studies linked the immune system to these diseases. In 1913, Friedberger[1] produced an immune arthritis experimentally. In 1933 - 1934 Klinge[1] et al following on Friedbergers findings, did a series of experiments that established an association between immune arthritis in rabbits injected with horse serum,

and the presence of fibrinoid material in the affected tissues. Shortly after in 1935 Klemperer et al[1] compared these findings with similar findings in blood vessels of patients with systemic lupus erythematosus and systemic sclerosis and in 1942 in a landmark article[2] reviewed the exisisting findings and theories. They postulated that the widespread occurrence of zones of injury to collagen tissue and in particular the frequency of fibrinoid degeneration in systemic sclerosis and acute systemic lupus erythematosus could be viewed as a primary disorder of the collagen tissue system and the variable manifestations could be explained on this basis in these two clinically distinct entities, and that hypersensitivity played a major part. Soon after, Rich and Gregory in 1947[1] obtained evidence that polyarteritis nodosa, a condition in which fibrinoid material was found in visceral arterial lesions could be attributed to hypersensitivity and could be experimentally reproduced by hyperimmunising rabbits with foreign serum.

The relationship to serum antibodies was first demonstrated in 1955. Ackrod[2] found plasma proteins with the properties of antibodies in the fibrinoid material, and administration of Serdomid to rabbits was followed by a purpura with tissue damage fibrinoid in nature which was associated with specific precipitating antibodies. In 1956 Gardner[1] correllated

levels of plasma globulins with levels of plasma cells in rheumatoid arthritis. The following year Carpenelli[1] described antibodies to DNA and Franklin[1] showed the LE cell phenomenon described earlier in 1947 by Hargreaves[1] to be due to antibodies to DNA - histone complex. Anti nuclear antibodies were first described in rheumatoid patients by Holman and Datcher[1] who found that amongst the raised plasma globulins were abnormal antibodies that reacted with nuclear chromatins and soon after these antibodies were described in systemic lupus so that by the 1960's the link between immune phenomena and these diseases was well established, first because of the finding of abnormal globulins and secondly because of the good response to steroid therapy.

Subsequent developments have mainly been elaborations on these initial findings. As new techniques and laboratory methods develop numerous subsets of anti nuclear antibodies have been discovered including the discovery of extractable nuclear antibodies which led to the description in 1972 by Sharp[3] of a new, related clinical entity - the mixed connective tissue disease.

Review of the African Literature.

In the late 50s and early sixties, rheumatoid arthritis and related connective tissue disorders were generally considered to be uncommon; infact all diseases of autoimmunity were thought to occur infrequently.[4] In recent years, however some of these

Views have changed considerably especially towards rheumatoid arthritis which has been established as being similar clinically and immunologically to the rheumatoid arthritis in the Caucasians[5,6] However, little has been written on lupus erythematosus still less on scleroderma and dermatomyositis.

The Kenyan Situation.

The first significant report was by Hall[7] in 1966. He studied the clinical patterns of arthritis and related disorders in in-patients at Nakuru General Hospital over 18 months and found amongst his cases 8 patients with rheumatoid arthritis and 3 with systemic lupus erythematosus but he never saw a case of scleroderma. His study was limited by the fact that the patients had to be ill enough to require admission in the face of more serious life threatening diseases as are to be found in a hospital like Nakuru. However from his clinical experience generally, he saw only three cases with systemic lupus erythematosus although locally it was quite well described. The only probable case of Dermatomyositis he ever saw may have been trichinosis. Since then Otieno[8] et al in 1985, have reported 31 cases from a retrospective study of patients seen at Kenyatta National Hospital between 1972 - 1984. This review suggested that systemic lupus erythematosus was seen in younger population groups here.

East and Central Africa.

In 1961 Shaper[9] reported five cases of systemic lupus erythematosus he saw just after the LE preparation method became available locally. In his report he described in detail the clinical presentation to illustrate the diversity of the presenting features in Ugandan Africans. Recently (1980) Kanyerezi[10] described twenty one cases he had seen over eleven years in Uganda. His cases were relatively severe compared to other series and included four deaths due to central nervous system, Renal and Cardiac complications. The incidence of butterfly rashes and renal involvement was high but haematological features were relatively uncommon and there was a high incidence of unexplainable eosinophilia.

From Ethiopia Teshale[11] et al 1984, reported 16 patients seen in Addis Ababa in four years without any remarkable clinical features. Surprisingly, in Central Africa, Gelfund[12] et al reported in 1969 as having looked for and failing to find a single case of systemic lupus erythematosus in a five year prospective study.

West Africa.

Between 1956 and 1966 Basset[13] in Dakar did a 10 year prospective study on "collagenoses". He saw 72 possible cases in a dermatology clinic. Twenty one he dismissed and 6 were of uncertain diagnosis. He found discoid lupus to be relatively common in young normadic adults aged between 20 - 30 year but he only saw one case of the systemic form. He mentions having

seen some patients with dermatomyositis who presented with pruritus, general malaise and "erythroderma". The six cases of scleroderma he saw presented differently from the recognised form described in Europe and America and the disease in the Europeans residing in the same region. Pruritus, hypopigmentation and achromic spots were prominent features as was muscular atrophy and weakness, as if they were variants of dermatomyositis ('sclerodermatomyositis'). Jackyk's (1976) [14] case had similar presentation, and the differential diagnosis was leprosy. Ladipos (1976) [15] case in Nigeria was treated for a long time as leprosy. Then more recently Somarin [16] (1981), and Monnier [17] 1985 have reported one and eleven systemic lupus erythematosus cases respectively.

Southern Africa.

In a large hospital for Blacks and Indians and over six years Seedat (1977) [18] reported having seen 13 Blacks with systemic lupus erythematosus and that the disease was typical in presentation except that he did not find it in children and neither had Jessops [19] in 1973 (he had found systemic lupus erythematosus in 8 adult blacks and 86 coloured). Rovers (1981) [20] also did not find systemic lupus erythematosus in Black children in one of the largest hospital for Blacks in Johannesburg in five years. Recently Lutalo [21] (1985) came across 3 cases of systemic lupus erythematosus in a peripheral Zambian hospital.

Dermatomyositis is said to be common amongst Blacks in Southern Africa as is scleroderma in Blacks who work in the mines.[22]

The above reports would seem to suggest that these disorders are indeed unusual and where systemic lupus erythematosus does occur the clinical presentation does not differ markedly from the disease elsewhere but that scleroderma probably does.

In 1962, Greenwood made the observation that autoimmune diseases were rare in Africans. He thought that probably chronic parasitic infections played a protective role and he domonstrated this experimentally with NZB and NZW/NZB hybrids infected with malaria.[4] Even from the relatively medically advanced South African society, the incidence of systemic lupus erythematosus is small in Blacks but comparatively higher in Whites. The drug induced lupus syndrome has not been described in Blacks there. Seedat[17] found one possible case related to Isoniazid in a coloured woman. Perhaps the absence of cases related to hydrallazine can be explained on the genetic basis, Africans in general being fast acetylators. On the other hand systemic lupus erythematosus could be commoner in the milder forms (Fessel - mild cases are commoner than the severe classical type).[23] Kanyerezi[10] and Lutalo[21] both suggest that perhaps we are missing the milder cases. Perhaps it is a lack of awareness, after all the majority of Africans are seen in small peripheral health institutions, basically staffed, and certainly without facilities for detecting LE cells or antinuclear antibodies.

Ladipo's case of progressive systemic sclerosis was managed for a long time as leprosy; all of Otieno's cases had a butterfly rash-could it be that systemic lupus erythematosus was thought of only after the appearance of that rash? Shaper's[19] five cases all presented very differently and indeed his report was partly to illustrate this diversity. Basset saw in his patients with scleroderma, certain features which are not seen in Caucasian patients in the same population. So it is possible that these disorders are overlooked or misdiagnosed in the midst of the "malarias" of Africa. Discoid Lupus would seem obvious but reports are few (so are dermatology facilities) and since it is not a disabling disease perhaps patients do not readily seek treatment.

There is a big descrepancy in the incidence of systemic lupus erythematosus in Blacks in Africa and Blacks in the U.S.A.[23] and West Indies.[24] In Jamaica the finding of a defect in the lymphocytes in families of three people with systemic lupus erythematosus and related disorders may turn out to be a manifestation of a "genetic predisposition"[25]. Jessops[19] found the frequency of systemic lupus erythematosus in coloured people very much higher than in Blacks. It is a fact that in America and West Indies "Coloured" people in the South African sense, are termed as "Blacks".

Aspects on aetiology and pathogenesis.

The three current theories on the pathogenesis of scleroderma - vascular, immune and abnormality of collagen metabolism are summarised by Lee E.B. et al (1984)[26]. Systemic lupus erythematosus has been linked with endocrine, genetic and the most plausible-an environmental factor - probably a virus modified by endocrine and genetic factors. In support of the virus theory is the finding of virus like particles in active Discoid lupus lesions (but not in burnt out lesions) and the similarity of systemic lupus erythematosus to the diseases of Aleutian Mink[27] systemic lupus in dogs and NZB/NZW hybrids, whose causal relationship to specific viruses has more or less been established[28]. Rheumatoid arthritis has been linked with a number of organisms but their pathogenic role is uncertain.

It has been many years since it was demonstrated that sera of patients with systemic lupus erythematosus and related diseases reacted with nuclear antigens and an immunologic pathogenesis presumed. Since then numerous antigen systems recognised by antinuclear antibodies[29] have been discovered and efforts made to characterise one antibody marker to one disease for diagnostic purposes and some have been accepted as markers. However the actual role of these abnormal antibodies in the aetiology of the disease remains unresolved. Antidouble stranded DNA/DNA complexes which have been eluted from nephritic kidneys are thought to be involved in its pathogenesis. The other

possible way tissue damage may occur is when antigen-antibody reactions activate complement and/or by antibody dependent lymphocytotoxicity. But the role of abnormal antibodies e.g. rheumatoid factor occuring in normal individuals without the development of symptoms is uncertain.

The association of antinuclear antibodies with these diseases is indisputable even though their role is uncertain. Currently the focus is now on studies on B cell clones[30] and their part in the pathogenesis.

Materials and Methods

This study was done at Kenyatta National Hospital, on all the patients encountered with lupus erythematosus dermatomyositis and scleroderma at the Dermatology clinic, medical and dermatology wards. A circular was also sent out to the outpatient filter and casualty departments requesting that any persons suspected to be having these disorders should be referred to the Dermatology clinic or to the author.

Patients already diagnosed and on follow up as well as new patients were included in this study. The history and physical examination were done and blood specimens taken for analysis. The findings were recorded in a questionnare. (see appendix 1.)

History and physical examination.

A detailed history was taken with the aim of trying to establish the earliest symptoms and the progression of the disease, any precipitating factors etc; (Appendix 1 questionnare) as well as a systemic enquiry on the current symptoms. A physical examination was then done and systemic and cutaneous findings documented. Reference was made to the patients' medical records in the cases where patients were already on follow up and the initial clinical findings, clinical and pathological findings during the period of follow up, treatment and response to treatment were documented.

Investigations.

Blood specimens were taken for complete haemogram ESR, urea and electrolytes, urinalysis, LE cells, antinuclear antibodies, kahn test, complement immunoglobulin and immune complex profiles. Biopsies were taken for confirmation of diagnosis where indicated. Radiological studies - chest xray (on all patients), barium swallow and meal and x-ray of hands and feet were done when indicated. Blood taken for analysis of immunological profiles was separated immediately and stored at $-70^{\circ}C$ for later use.

Methods used.

Standard methods were used for the assay of urea and electrolytes, haemogram and ESR, Le cell demonstration and Kahn test. Platelet count was done by Thrombocoulter. Urinalysis was assayed for protein by dipstick method using standard uristicks. Antinuclear antibodies were demonstrated by the indirect immunofluorescence test using rat liver as substrate. Screening on all sera was done at 1 in 10 dilution and titres were estimated by doubling dilution technique. Complement and immune complex assays were also done. C_3 C_4 C_{1q} lgm and lgA immune complexes were assayed by the polythylene Ethylene Glycol (PEG) precipitation method. Quantitative determination of Human lgG, lgA, lgM was done using the Radial Immunodiffusion (Mancini) technique.

Controls.

Control sera was taken from fifty seven healthy females of child bearing age. Sera was also taken from twenty four rheumatoids with classical or definite disease.

Criteria for diagnosis.

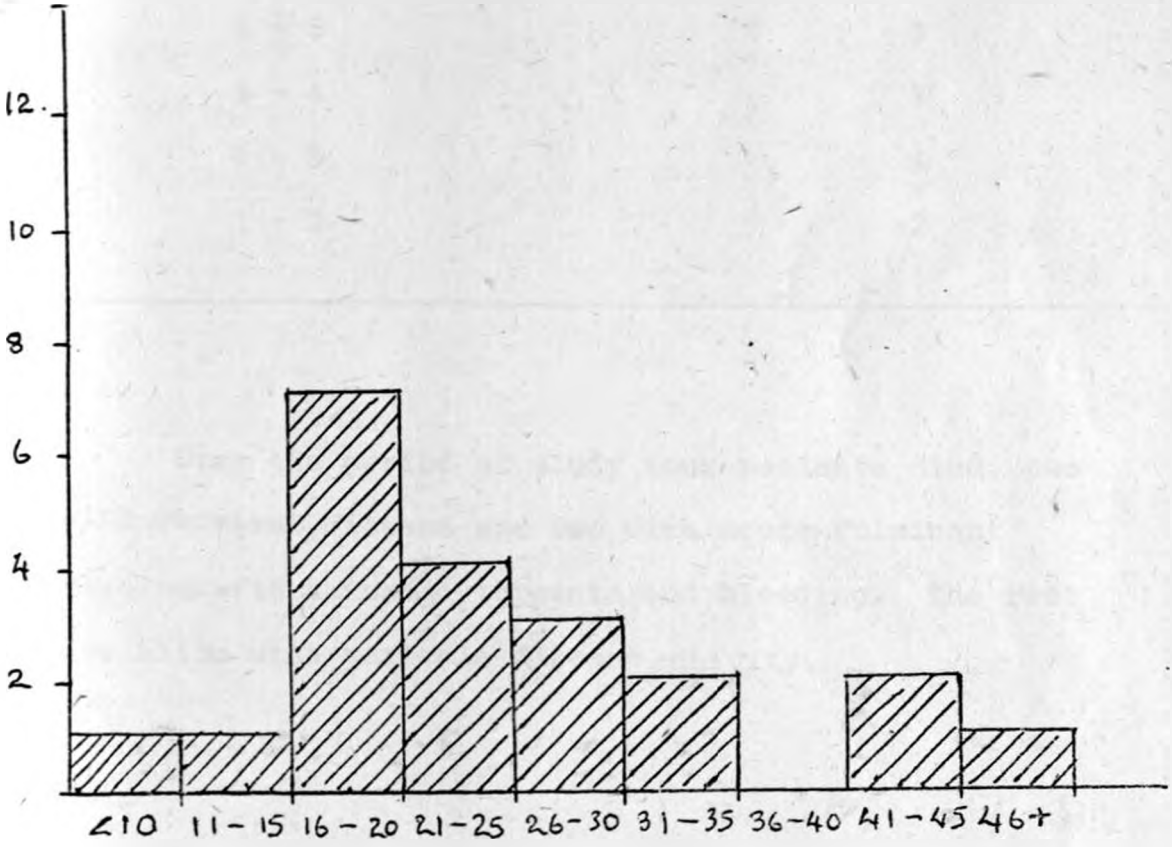
All systemic lupus patient fulfilled the American Rheumatism (1982) criteria for diagnosis (see appendix III). All dermatomyositis were classified by the criteria offered by Bohan and Peters (appendix IV). Systemic scleroderma was diagnosed by the criteria offerred by the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee (1980) (appendix II) and Rheumatoid arthritis classified by the ARA criteria for diagnosis of Rheumatoid arthritis 1958 (appendix V.)

A total number of 127 patients and controls were seen and have been included in the study. Twenty had systemic lupus erythematosus, 13 scleroderma, 3 dermatomyositis, 11 Discoid lupus, 24 rheumatoid arthritis patients and 57 controls.

Results.

I Systemic Lupus Erythematosus.

A total of twenty three patients with antinuclear antibodies were studied. Twenty of these patients fulfilled the 1982 American Rheumatism Association Criteria (see appendix II) for diagnosis. All the patients were famales, and their ages ranged from 8 years to 47 years with most of them falling between 16 and 35 years.



1.1. Histogram showing the age at onset of systemic lupus erythematosus.

Table 1.2. Systemic lupus erythematosus duration of the disease at the time of examination.

Duration of disease	No of patients
5 years	6
4 - 5	3
3 - 4	3
2 - 3	4
1 - 2	2

Over the period of study four patients died, two with cerebral disease and two with acute fulminant disease, with thrombocytopaenia and bleeding. The rest are alive with variable disease activity.

Table 1:3 Systemic lupus erythematosus clinical manifestations.

Clinical features	No of patients	%
Arthritis	19	95
Dermatological manifestations	18	90
Weight loss	18	90
Headache	17	85
Abdominal pain	14	70
Lymphadenopathy	14	70
Renal abnormalities	13	65
Pleuresy	13	65
Facial swelling	12	60
Haematological abnormality	11	55
Weakness	11	55
Psychosis	9	45
Hypertension	6	30
Depressive features	5	25

Systemic lupus erythematosus.

Table 1.4: Dermatological manifestations.

Dermatological feature	No	%
Erythematosus rashes	17	85
Malar rash	17	85
Photosensitivity	15	75
Mucous membrane lesions	11	55
Alopecia	11	55
(Other hair changes)	10	50
Raynauds phenomenon	8	40
Discoid rash	5	25

Eighteen patients were observed to have at least one dermatological feature. The erythematous rashes which were observed are erythematous annular lesions, annular lesions with central necrosis (vasculitis rash) erythematous macules, flaccid bullous lesions healing with post inflammatory hypopigmentation without scarring, erythema multiforme, erythema annulae centrifugum (annular lesions with a peripheral rim of flaccid bullae) and bullous pemphigoid.

Ten patients (50%) were observed at one time or other to have lupoid hair (fine straight hair) and one patient's hair became acutely grey.

The diagnosis of systemic lupus was not immediately apparent and the following table shows the main differential diagnosis.

Table 1:5 The main differential diagnosis of systemic lupus erythematosus.

Idiopathic thrombocytopenic purpura
Epilepsy
Puerperal psychosis
Pyrexia of unknown origin
pneumonia
acute discoid lupus erythematosus
photosensitive dermatitis
pemphigus foleaceous
erythema multiforme
erythema annulare centrifugum
Chronic Bullous disease of childhood.

Table 1:6. Systemic Lupus Erythematosus

The frequency of the initial presenting symptoms.

Symptoms	Frequency	%
Butterfly rash	5	25
Pruritis	5	25
Alopecia	4	20
Erythematous rashes	4	20
Erythematous bullous rash	3	15
Epileptic fits	2	10
Photosensitivity	2	10
Discoid rash	1	5
Mouth ulcers	1	5
Epigastric pains	1	5
Pain in neck	1	5
Cough	1	5
Headache	1	5
Lupoid hair	1	5
Nasal bleeding	1	5
Facial swelling	1	5

Vague body pains, weight loss, chills and weakness were common accompaning features to the presenting symptoms. The weakness in some cases was profound and was described as being so severe as to render the patient bedridden over months on end. Erythematous skin lesions, alopecia and pruritus occurred in 17 patients as an initial presentation. A feature of interest is the occurrence of bullous lesions only over the involved joints. Loss of hair as an initial symptom occurred in 4 patients while in 3 patients pruritus was a major feature at the time of presentation. In five of these patients the initial presentation of the disease was precipitated by pregnancy and the disease manifested itself around the time of delivery. The presentation was in the form of erythematous rashes and pueperal psycosis. An unusual complaint which was almost universal was that of frequent sore throat associated with cervical lymphadenopathy which tended to be self limiting.

Clinical summaries of cases of interest

Case 1.1

P.O. age 18 female

was admitted to labour ward with a history of loss of fetal moveme nt and "skin rashes" where she delivered a macerated term fetus. She subsequently developed a very high fever, was very ill, lost all her scalp hair and had widespread bullous skin lesions some of which were haemorrhagic and she was also thrombocytopenic. Investigations failed to demonstrate an infective cause and she was non response to antibiotic and antimalaria therapy. She was later diagnosed as having systemic lupus erythematosus and responded initially well to prednisone 60mg daily in divided doses. She however relapsed and later developed a severe bleeding tendency and confusion and died 6 months after diagnosis.

Case 1.2

R.M. age 9 F.

developed epilepsy 6 months before presentation at the dermatology ward with a bullous skin rash and fever. A diagnosis of chronic bullous disease of childhood was made. During her admission she was noted to have a blood stained sputum which was negative for acid fast bacilli three times.

Chest xray showed hilar lymphadenopathy. She had lupoid hair and was psychotic and complained of severe generalised body pains. The fever persisted but eventually settled on its own. A histology report of bullous pemphigoid was made. Subsequently she was started on anti Tb.treatment and prednisone and discharged. She was readmitted 9 months later with the same symptoms, this time with addition of arthritis. Chest xray was again normal. She improved on prednisone 30mg. On her third admission in September, 1985 she presented again with bullous ulcers in the mouth, epistaxis, fever, arthritis and chest pain. This time she had a butterfly rash and palmar erythma. Antinuclear antibodies and LE vells were positive and she was diagnosed as having systemic lupus erythematosus. Again she improved on steroids.

Case 1.3

P.N. Age 12 F.

was well up to October, 1985 when she developed blistering lesions over the knee joints which healed by themselves. One week before admission in December she had an acute onset of general malaise, fever and joint pains. She was admitted with a diagnosis of pyrexia of unknown origin. A septic screen was not forth-coming. She developed a butterfly rash and antinuclear antibodies and LE cells were positive complement levels

were reduced and abnormal immune complexes and proteinuria were demonstrated. She was started on prednisone and discharged. She was readmitted with widespread skin rashes and a productive cough with blood stained sputum. Acid alcohol fast bacilli were demonstrated in the sputum.

Case 1.4.

S.W. age 22.

present in 1981 with butterfly rash. Systemic lupus was diagnosed and she was put on steroids She was readmitted frequently in relapses and widespread infection of skin lesions. In 1985 she was admitted with skin lesions and prednisone was stepped up to 60mg daily. She developed psychosis which improved on anti-psychotic therapy. She died suddenly on a subsequent admission after an epileptic fit.

Plate 1 & 2

Systemic lupus erythematosus

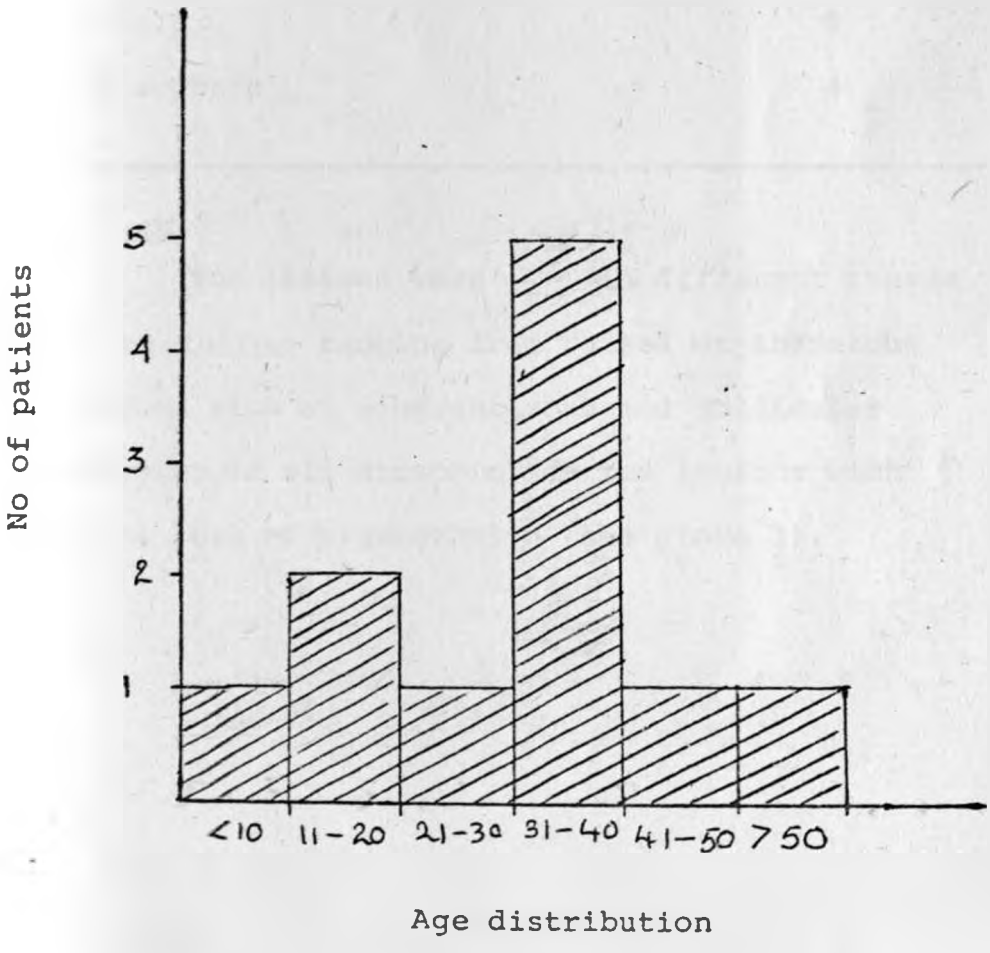
malar rash and

erythematous rash

Palmar erythema.

II Discoid Lupus Erythematosus

Eleven patients, four males and seven females had clinical or clinical and biopsy proven discoid lupus.



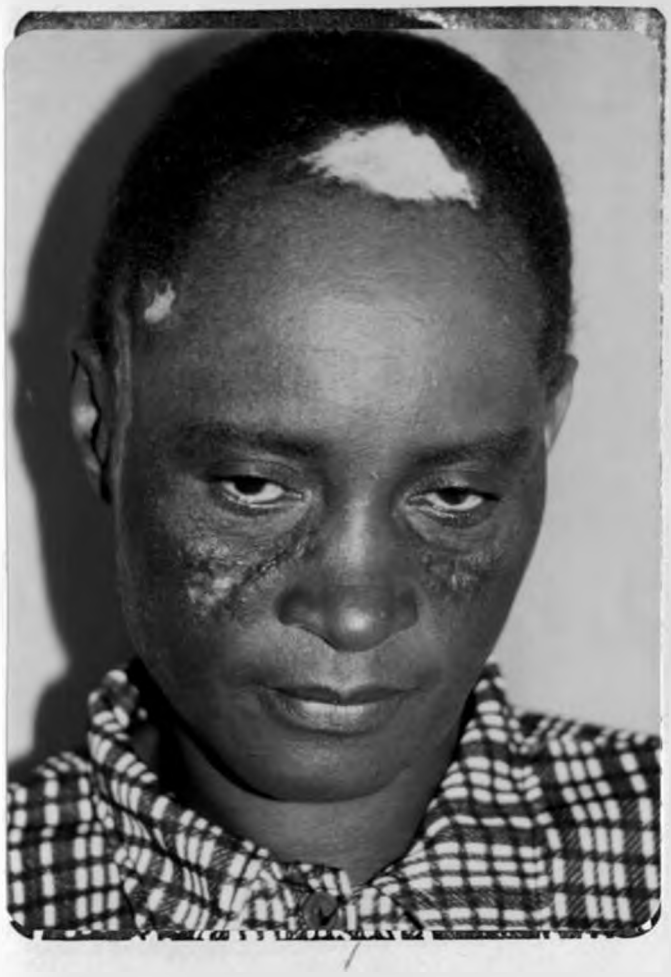
Histogram 2:1. Age distribution of patients with discoid lupus.

Table 2:2. Discoid Lupus Erythematosus site of involvement.

Site	Frequency
face	10
ears	9
scalp	5
elsewhere	4

The lesions were in different stages of evolution ranging from raised erythematous plaques with an adherent scab and follicular plugging to old atrophic scarred lesions with total loss of pigmentation (see plate 3).

Plate 3.



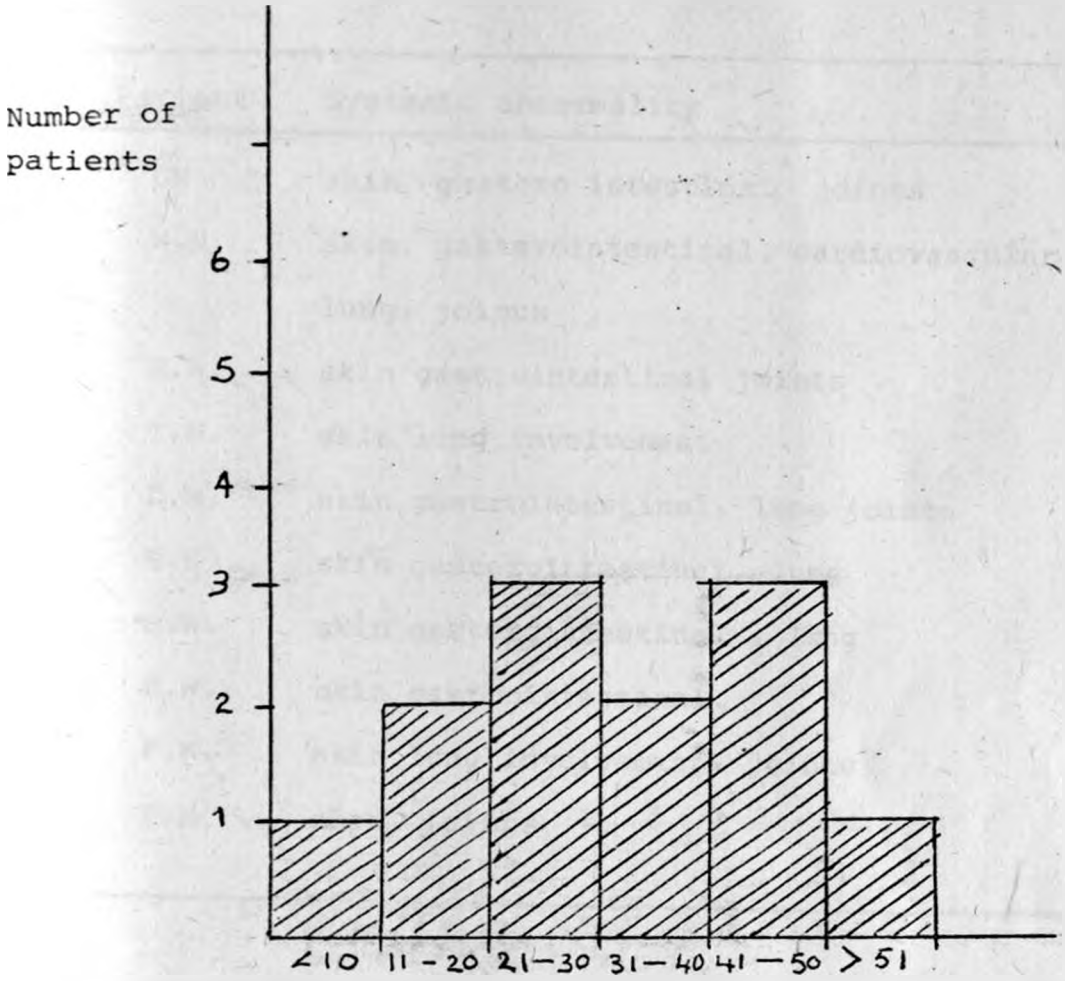
Discoid lupus erythematosus butterfly rash, scalp and preauricular involvement with scarring.

Scleroderma.

A total of thirteen patients were seen with scleroderma (sclerosis). 4 males and 9 females.

Table 3.2. Clinical types of scleroderma

Patient	Age(yrs)	Sex	Duration of symptoms in years.	Clinical type
G.N.	23	M	1	Systemic sclerosis
W.N.	58	M	4	Systemic sclerosis
E.W.	47	F	4	Systemic sclerosis
T.M.	59	F	9	Systemic sclerosis
D.M.	55	M	11	Systemic sclerosis
R.K.	32	F	11	Systemic sclerosis
S.W.	35	F	3	Systemic sclerosis
R.W.	22	F	3	Systemic sclerosis
P.K.	50	F	6m	Systemic sclerosis
Z.W.	26	F	9m	Multiple plague morphea
P.M.	30	M	9m	Systemic sclerosis
F.W.	18	F	9	Linear morphea
A.M.	9	F	1	Multiple plaque morphea



Age in years.

Histogram = scleroderma. Age at onset of symptom

The range was from 9 years to 55 years. The duration of symptoms between 6 months to 11 years.

Patient	Systemic abnormality
GN	skin, gastero intestinal joints
W.N.	skin, gasterointestinal, cardiovascular lung, joints
E.W.	skin gastrointestinal joints
T.M.	skin lung involvement
D.M.	skin gastrointestinal, lung joints
R.K.	skin gasterointestinal, lung
S.W.	skin gasterointestinal , lung
R.W.	skin gastrointestinal.
P.K.	skin lung involvement, joints
P.M.	skin, joints

Table 3.2: Systemic involvement in diffuse scleroderma.

The three patients with plaque and linear morphea had no evidence of increased lung fibrosis or any other systemic involvement.

The dermatological manifestations in scleroderma.

Table 3:3.

Dermatological feature	No.	%
Skin sclerosis	13	100
face	10	
chest trunk	5	
hands arms	10	
legs	6	
Raynaulds phenomena	10	77
Diffuse hyperpigmentation	8	61.8
Poikilodermatous changes	7	53.8
face	3	
trunk	4	
limbs	4	
Hair thinning or alopecia	5	38.9
Finger tip ulcerations	5	38.9
Morphea plaque	2	15.9
linear	1	8

In the Dermatological manifestations of scleroderma presenting symptoms were variable. In seven patients the first symptom was Raynauds phenomena and swelling of the fingers and five of these patients had fingertip ulcerations. There was diffuse increase in pigmentation of the affected area before the sclerosis was noticed in most of the patients and in one patient this was accompanied by intense pruritis.

Table 3:4 The presenting features in scleroderma.

Presenting feature	Frequency in 13 patients	
Raynauds	7	54%
Swelling of digits	5	38
Pruritis	3	23
Arthralgia	2	16
Increase in pigmentation	2	16
Poikiloderma	1	7%
Acrosclerosis	1	7
Fingertip ulcers	1	7
Alopecia	1	7
Tighness of skin	1	7
Swelling of feet	1	7
Difficulty in swallowing and phonation	1	7
Papular rash	1	7
Pain	1	7
Abdominal swelling	1	7
Linear sclerosis	1	7

It was difficult to pin point the point in time when skin sclerosis began.

Case reports of patients with interesting clinical features.

Case 2.1.

E.W. age 47, female. Presented with 3 year history of pruritis and abdominal distension and discomfort and complaints of frequent passage of flatus and diarrhoeal stool. She was seen in various clinics including a psychiatric clinic where she had been referred for depression before the skin sclerosis was noticed. She had extensive gastrointestinal involvement with malabsorption and gross gaseous distension and had lost a lot of weight and she was extremely weak.

Case 2.2.

W.N. age 58, male. Presented with a three year history of selling of hands and tightening of the skin around the fingers which eventually involved the face, trunk and lower limbs. He also complained of weight loss cough muscle weakness, joint pains and swelling of the abdomen on and with regurgitation of swallowed food or food being stuck at the neck region on swallowing. Barium studies showed involvement of the oesophagus, chest xray showed lung fibrosis and cardiac enlargement. A needle EMG was myopathic. Echocardiogram showed a small pericardial effusion with left ventricular dilatation.

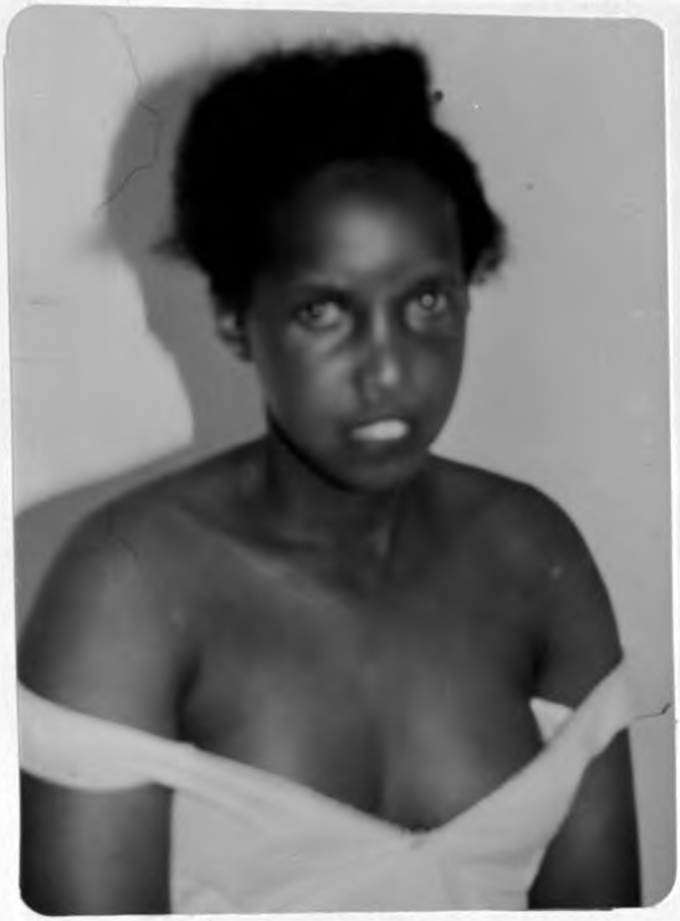
Antinucleolar ancibody was demonstrated. Skin involvement was that of classical scleroderma including multiple punctuate ulceration of finger tips and poikilodermatous changes in a background of diffuse hyperpigmentation.
His illness was progressive from time of diagnosis and he died in cardiac failure.

Case 2.3:

A.M. Age 11 years F.

Was well until 1985 when she complained of pain and pruritis in multiple sites on the trunk and thighs followed by an increase in pigmentation and skin atrophy in the same site with the lesions spreading radially. She had no systemic complaints. On examination she had large areas of plaque morphea on both thighs with patches of infiltrated hyperpigmented pruritic areas on the trunk and upper limbs and neck. (see plate 11).

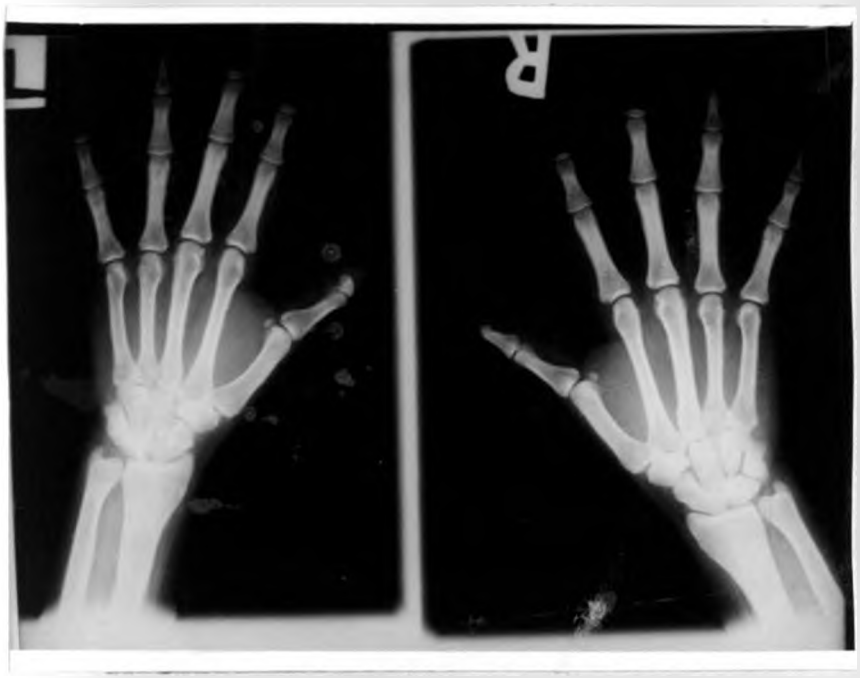
Plate 4 & 5



Scleroderma with hemifacial atrophy.

cleroderma swollen
horted digits in
and involvement.

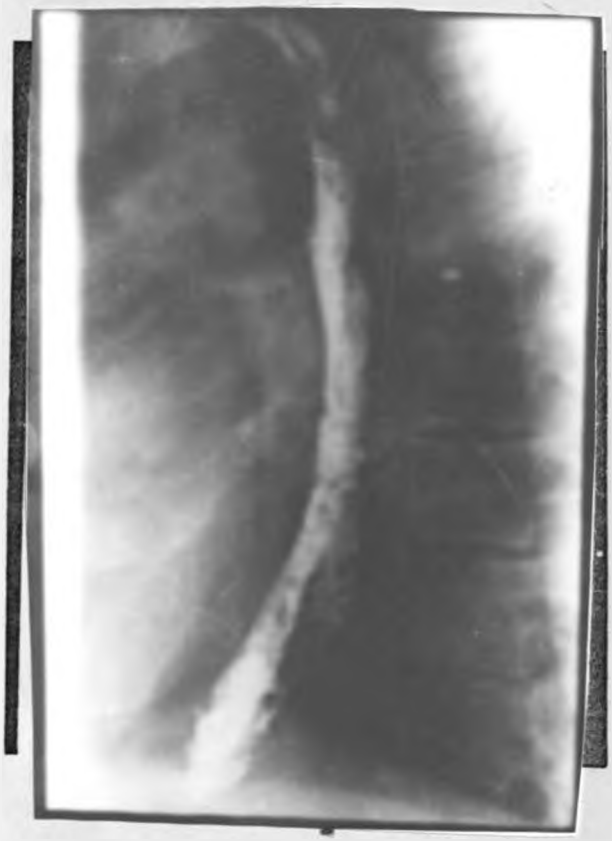
Plate 6



Scleroderma - resorption of the terminal tufts.

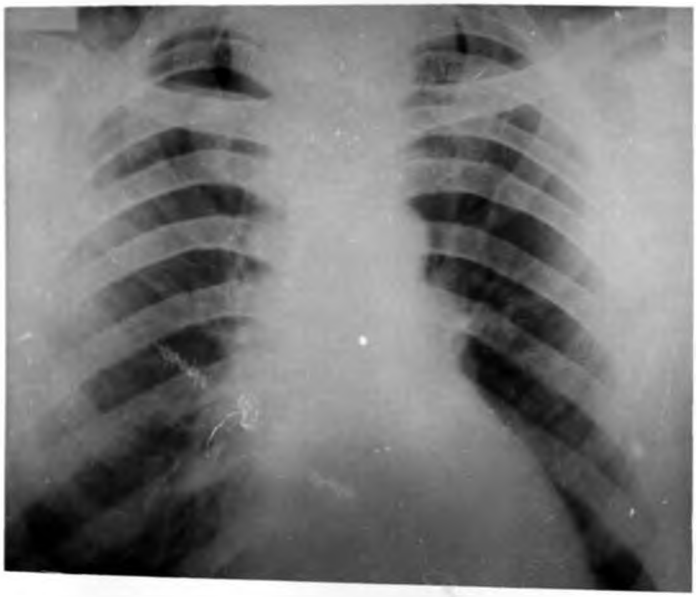
Plate 7

Scleroderma eosophageal involvement.



Scleroderma - failure of eosophagus to collapse after emptying.

Plate 8



Scleroderma interstitial lung fibrosis with flattening out of the diaphragm.

Plate 9

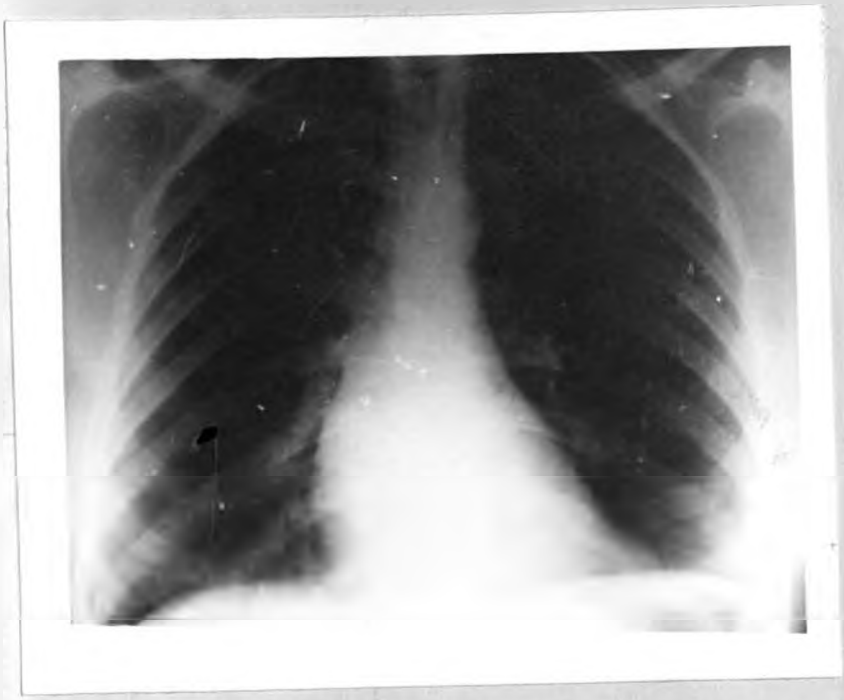
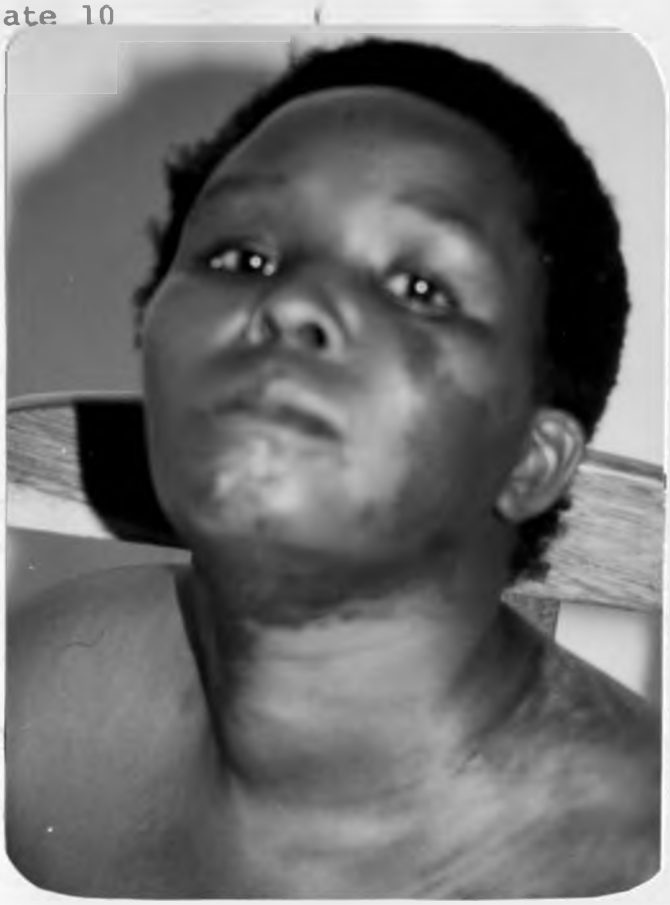
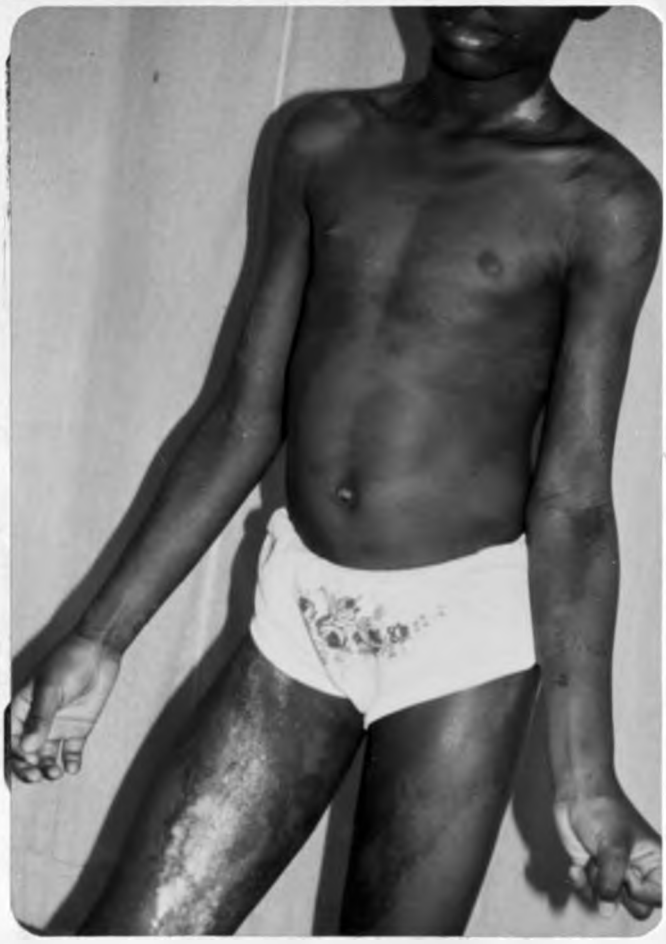


Plate 10



Multiple plaque morphea.

Plate 11



Multiple plaque morphea.

IV Dermatomyositis.

Three patients were diagnosed as having dermatomyositis. Two were males and one female and fell into the classification of definate probable and possible dermatomyositis.

Patient	Age	Sex	Duration	Classification
Z.G.	30	M	1 yr	Probable
M.W.	42	F	12 yrs	Definate
J.K.	56	M	3 yrs	Possible

Table 4.1: Classification and aged of the patients with dermatomyositis.

Case report 3.1:

M.W. Age 42 F. Presented at the age of 30 years at the E.N.T. department with hoarseness of the voice for several years before the appearance of heliotrope oedema and muscle weakness creatinine phosphokinase levels were raised and she had a myopathic EMG and a barium meal showed normal mucosal pattern with abnormal peristaltic movements. Antinuclear antibodies were demonstrable. She responded to steroid therapy and remains well but with complaints of weakness on and off. She is on a maintainance dose of 5mg prednisone daily.

PLATE 12 ECG of a patient with scleroderma showing ventricular ectopics.

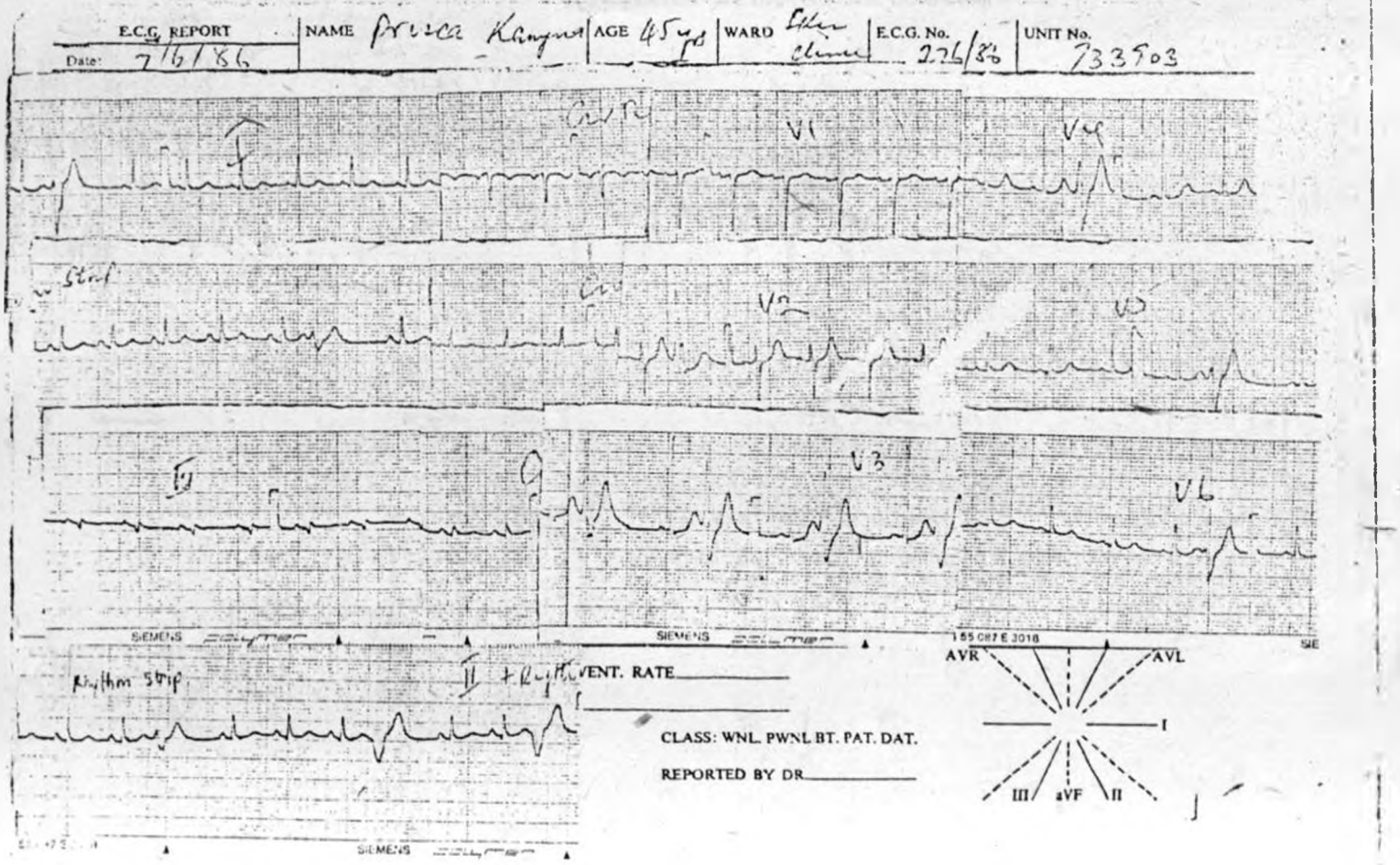
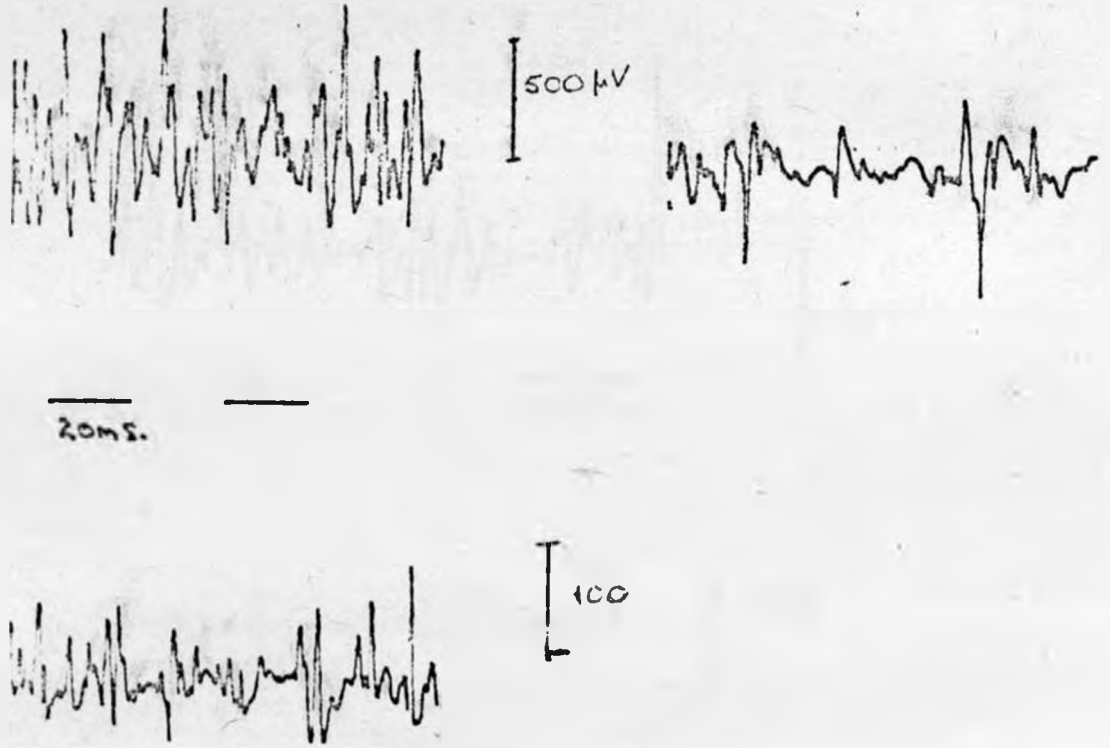


Plate 13

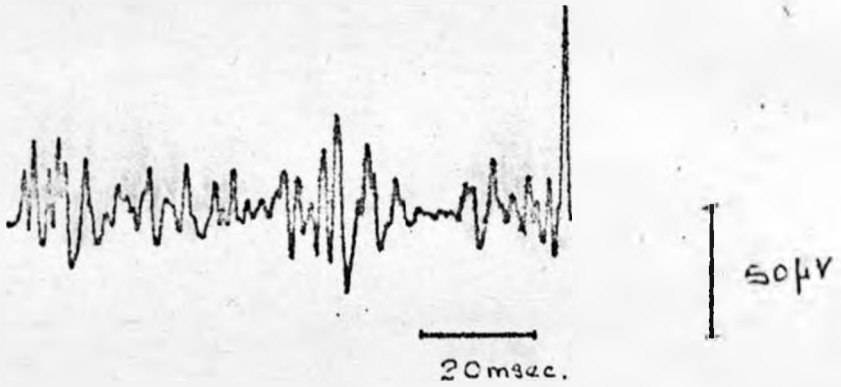
Electromyograph - showing normal and abnormal muscle activity in the same patient with scleroderma.



Mary Wangui 55C-32
F-42

Plate 14

Electromyography - myopathic changes in Dermatomyositis



Nerve Conduction

RM = 63 ms^{-1}

RU = 64 ms^{-1}

Sensory

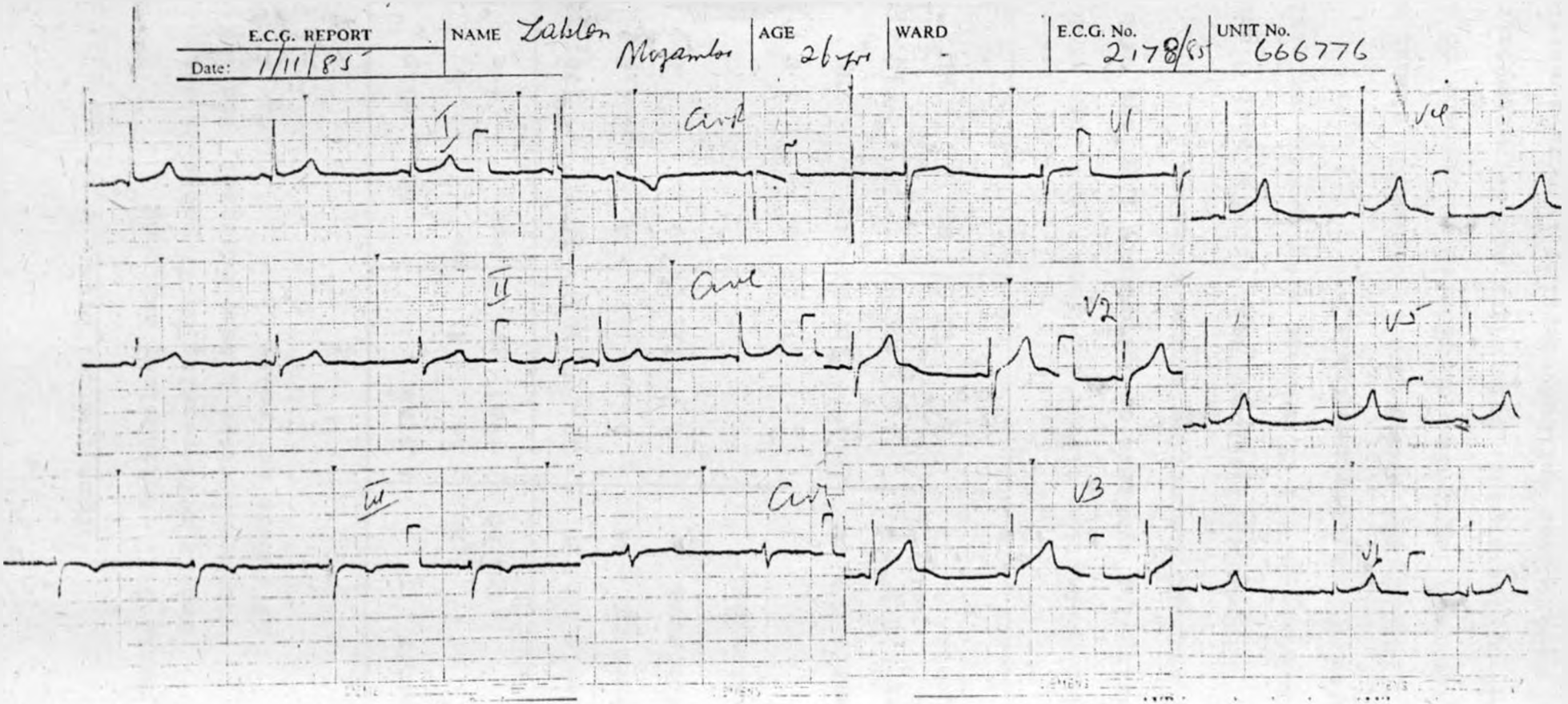
Latency 3·1 msec

Rise time 0·7msec

Amplitude 60μV.

Plate 15

Sinus bradycardia in Dermatomyositis



Immunological Data.

Table 5:1. Antinuclear antibody and LE cell results on 77 patients seen with connective tissue diseases, and 57 female controls.

Disorder	No Tested	A.N.A. no +ve	A.N.A. % +ve	LE cells no +ve	LE cells % +ve	P Value
Systemic LE	20	20	(100)	14	(70)	$P < 0.001$
Discoid LE	11	0	(0)	0	(0)	$P < 0.001$
Scleroderma	13	3	(23.1)	0	(0)	
Dermatomyositis	3	1	(33.3)	0	(0)	
Rheumatoid A.	24	4	(16.6)	ND	ND	
Other C.T.D*	6	4	(66.6)	1	(16.6)	
Controls	57	2	(3.5)	ND	ND	

* Other connective tissue diseases - patients with overlapping symptoms or laboratory findings with ill defined connective tissue diseases.

Antinuclear antibody test is of utmost diagnostic importance in all CT disease with special emphasis on systemic lupus erythematosus.

The LE cell phenomenon is obsevable almost exclusively in systemic lupus when considered in respect to discoid lupus erythematosus, scleroderm and dermatomyositis.

Antinuclear antibody testing is more sensitive than the LE cell phenomenon.

Table 5.2 Antinuclear antibody pattens on the +ve sera

Group	No tested	No +ve	Homogeneous	Granular	Speckled	Peripheral	Nuclear.
SLE	20	20	6	5	2	3	0
Scleroderma	13	3	0	1	0	0	2
Discoid LE	10	0	0	0	0	0	0
DMS	3	1					
RA:	24	4					
Controls	57	2	-	-	-	-	-

The Homogeneous, granular, speckled and peripheral pattens were observed in systemic lupus and Nuclear antibody in the scleroderma. One patient with scleroderma had a finely granular pattern.

Table 5.3 Antinuclear antibody titres and LE cell positivity in relation to the therapy of 18 systemic lupus erythematosus patients.

	Titre 1.10	1.20	1.40	1.80
untreated patients	1/5	-	1/5	3/5
	(1)	-	(1)	(3)
treated patients	6/13	1/13	3/13	3/13
	(4)	(0)	(1)	(3)

( ) denotes those which showed the LE cell phenomenon.

All 5 untreated patients had the LE cell phenomena while 8/13 (64%) of treated patients had LE cell phenomena. The LE cell phenomena shows no relationship to the Antinuclear antibody titre.

Table 5.4. A summary of the circulating immune complexes complement levels and total immunoglobulin abnormalities

Patient group	Number tested	Low Clq	Complement C3	Complement C4	Immune complexes IgG	Immune complexes IgM	Immune complexes IgA	Raised total Immunoglobulin IgG	Raised total Immunoglobulin IgM	Raised total Immunoglobulin IgA
Systemic lupus	(15	12 (80%)	9 (60%)	12 (80%)	10 (60%)	7 (47%)	9 (60%)	5 (33%)	2 (13%)	2 (13%)
Discoid lupus	5	1	1	0	2	3	3	0	1	0
Scleroderma	5	3	4	1	1	2	1	0	0	.0
Dermatomyositis	1	0	0	1	1	1	0	1	0	0
Others	4	3	1	1	3	1	0	1	0	0
Total	30	19 (63%)	15 (50%)	15 (50%)	17 (56%)	14 (46%)	13 (43%)	7 (24%)	3 (10%)	2 (6%
Controls	51	2 (4%)	1 (2%)	1 (2%)	0	9 (18%)	0	6 (12%)	15 (29%)	1 (2%

Table 5.5a. - Complement levels in the control group and the systemic lupus and combined connective tissue diseases group

	Control		Systemic lupus erythematosus			CTD. group combined		
	Range	Mean	Range	Mean	significance (p value)	Range	mean	Significance (p value).
Complement								
C_3	99-155%	125%	16-152%	84%	$p < 0.0001$	16-152%	10%	$p < 0.001$
C_4	79-117%	99%	22-100%	49%	$p < 0.0001$	22-100%	73%	$p < 0.0001$
Cl_q	98-164%	132%	13-110%	68%	$p < 0.0001$	13-100%	79%	$p < 0.0001$

* Range is within the 95% confidence limit.

Table 5.5b. Circulating immune complex values in the systemic lupus erythematosus, combined C.T.D. group and controls

	Control		Systemic lupus erythematosus				CTD group combined significance		
	range	Mean	Range	Mean	significance P value		Range	Mean	(p value)
Circulating immune complex									
lgG	0.2-0.8%	0.31%	0.9-4.8%	2.0%	P	0.001	0.9-4.8%	1.7%	$p < 0.001$
lgM	0-5.6%	0.99%	8.3-33%	7.9%	P	0.001	5.5-33%	7.4%	$P < 0.001$
lgA	-	-	-	-		-	-	-	-

* Ranges and means are not applicable as lgA circulating immune complexes are defined quantitatively as positive or negative.

Table 5.5c. - The total immunoglobulin values

	Control		Systemic lupus erythematosus			CTD. group combined		
	Range	mean	Range	mean	significance p value	Range	Mean	significance p. value
Total Immunoglobulin	IU/ml	IU/ml	IU/ml	IU/ml		IU/ml	IU/ml	
lgG	264-456	214	125-680	413	$p < 0.01$	125-680	343	$p > 0.10$
lgM	217-350	360	155-520	289	$p > 0.10$	155-520	362	$p < 0.05$
lgA	168-262	283	135-310	210	$p > 0.10$	75 - 360	207	$p > 0.01$

* Range is within the 95% confidence. limit.

There was a statistically significant difference in both the circulating immune complex and complement levels between the control group and the combined connective tissue study group and also between the systemic lupus erythematosus group and the control ($p < 0.001$ - $p < 0.0001$).

With the total immunoglobulin levels there was no statistically significant difference in the total lgG and lgA between the controls and the CTD study group ($p > 0.10$). There was however significantly higher levels of lgM ($p < 0.05$) in the C.T.D. study group as compared to the controls.

In systemic lupus erythematosus group the total lgA and total lgM values were not statistically different from those of the controls but total lgG levels were significantly raised ($p < 0.10$) compared to the controls.

Note

Rheumatoid arthritis was not included in the combined connective tissue diseases group.

Table 5.6a. Correllation between disease activity, complement, immune complexes and total immunoglobulins in untreated systemic lupus erythematosus patients.

Name	Clinical activity	ESR	ANA Titre	Lowered complement	circulating immune complexes	Total immuno globulins	Comment on immunological tests and clinical activity.
1. MO	++	48	1.80	C_4 C_3	lgG, lgA lgM	lgG	Circulating immune complexes with complement consumption - active disease.
2. LWT	++	40	1.40	Cl_q C_4 C_3	lgM lgA	lgM	Circulating immune complexes with complement consumption - active disease. Subsequently developed renal involvement.
3. EM	++ R	55	1.80	Cl_q C_4 C_3	-	-	Complement levels discordant with circulating immune complexes ? cryoglobulins with precipitation of immune complexes clinically remained active for a long time

Table 5.6a cont.

Name	Clinical activity	ESR	ANA Titre	Lowered complement	Circulating immune complexes	Total Immuno globulins	Comment on immunological tests and clinical activity
4. PM	++ R	62	1.80	Cl_q C_4 C_3	-	Not done	Circulating immune complexes with complement consumption. Active disease clinical activity increaased progressively to severe.
5 WSW	++	54	1.10	Cl_q C_4 C_3	lgA lgG	-	Circulating immune complexes with complement consumption. Active disease. Discoid lupus converted to systemic form clinically the disease fluctuates between active and quiescent disease.

* Clinical activity + - quiescent
++ - clinically active but not moribund
+++ - severe clinical disease
R - active renal involvement.

Table 5.6b: Correlation between disease activity complement immune complexes and total immunoglobulins in systemic lupus erythematosus patients on treatment.

Name	Clinical activity	ESR	ANA titre	Lowered complement	Circulating immune complexes	Total immuno-globulins	Comment on immunological tests and clinical activity
1.EO	+	22	1.10	C_4 C_3	lgG lgA lgM	lgG lgM	Circulating immune complexes with complement consumption - active disease clinically patient had active renal disease but other systems
2.JN	+	48	1.40	-	lgG	lgG,	Immune complexes but no consumption not active. She has renal involvement which was not active undergood immunosuppressant (azathiaprime and steroids control)
3.HBK	+	25	1.20	Cl_qC_3	lgG	-	Few circulating immune complexes and little complement consumption - clinically and immunologically in remission
4.FA.	++	30	1.20	Cl_q	-	-	Immunologically not active clinically was active - discordant results. Clinically flucuated from quiescent to mild disease activity.

Table 5.6b conti.

Name	Clinical activity	ESR	ANA titre	Lowered complement	circulating immune complexes	Total immuno globulins	Comment on immunological tests and clinical activity.
5. JAK	+++	53	1.80	Cl_q C_4 C_3	IgG IgA	IgG	Active disease with circulating immune complexes and complement consumption clinically was severely ill with anaemia thrombocytopenia and lupus pneumonitis
6. P.O.	+++ R	40	1.10	Cl_q C_4 C_3	-	IgA	Severe complement consumption - active disease. Required high dosages of steroids had thrombocytopenia later deteriorated and had severe fatal generalised disease and suspected Disseminated intravascular coagulation
7, AWK	++	30	-	Cl_q C_4	IgG IgA	-	Circulating immune complexes and complemen consumption - active disease discordant with the ANA which was negative at the time but positive before, but correlating with disease activity. Developed renal involvement later.
8. NW	++ R	ND	1.10	Cl_q C_4 C_3	-	-	Active disease but complement levels discordant with circulating immune complexe had acute renal involvement at this point improved gradually with residue renal disease.

Table 5.6b cont.

Name	Clinical activity	ESR	ANA titre	Lowered complement	Circulating immune complexes	Total immuno globulins	Comment on immunological tests and clinical activity.
9. S.W	++	46	1.40	C_4 C_3	lgG, lgM	-	circulating immune complexes with complement consumption - active disease. Clinically had frequent exercabations and cerebral disease.
10. LN	+ R	ND	1.80	C_4.	lgG, lgM lgA	-	Circulating immune complexes with complement consumption - active disease. Clinically only active renal disease.

Clinical activity + - quiescent
++ - clinically active but not moribund
+++ - severe clinical disease
R - active renal involvement.

Circulating Immune complexes and complement consumption correlated well with the over-all clinical disease activity, and also with renal disease activity when it occurred independently.

Low Cl_q, C_4, C_3 levels in combination was associated with increased and morbidity and mortality and had a good predictive value as to the course of the disease when it occurred in both the new patients and patients already on treatment. Low C_3 and C_4 combination was associated with good clinical recovery after institution of therapy in the new patients but with impending increase in disease activity in those already on treatment.

Cl_q, C_4 combination was seen in one patient also heralded increase disease activity.

Good clinical control was associated with low immunological activity.

Total immunoglobulin levels had no correlation with the disease status.

Discussion

Lupus Erythematosus, Dermatomyositis and scleroderma are uncommon diseases at the Kenyatta National Hospital. They are seen almost exclusively at the Dermatology clinic unless they are severe enough to warrant admission.

Systemic lupus erythematosus.

Twenty patients were seen during a period of one year who fulfilled the American Rheumatism Association Criteria for the diagnosis of systemic lupus erythematosus. 8 of them were newly diagnosed. Although this number is far smaller than that of Fessel[23] in San Franscisco and that of Wilson and Hughes[24] in Jamaica in terms of incidence, it was higher than that previously reported in Black Africa[8,18,11,10,21] All the patients were Black females most of them in the age range between 16-35 years. One was a child. This age range is comparable to that found in the Jamaica series[24] and the cases reported by Dubois.[39]

All the clinical features reported elsewhere were found in this series of patients but the occurrence of symptoms seemed to be comparatively higher. (Table 6.1. - a comparative analysis of the clinical features in patients with systemic lupus erythematosus).

Clinical feature	Present series	Wilson Hughes[20] (Jamaica)	Dubois et al[39]
	(21	(95)	520
Polyarthritis	95	89	91.5
Skin manifestations	90	58 (excluding alopecia)	71.5
Butterfly facial rash	85	32	50.7
Alopecia	55	70	21.3
Discoid lesion	25	14	-
Photosensitivity	75	12	-
Renal involvement	65	40	46.1
Pleurisy	65	32	45
Lymphadenopathy	70	40	58.6
Hypertension	30	-	25.2
Depression	25	16	25
Psychotic behaviour	45	16	-
Convulsions	10	3.15	13.8

Table 6.1 Systemic Lupus Erythematosus a comparison of the clinical features with other series.

The non specific symptom of fever and weight loss were noted in the majority of these patients. There was a high frequency of complaints of sore throat inframandibular swelling and cervical lymphadenopathy and "tonsillitis" occurring on and off, preceeding or coinciding with exercebations. In the Cairo-Glasgow study[33] sore throat occurred in 13 patients just before the onset of systemic lupus erythematosus and was associated with lymphadenopathy. It was thought that either reaction to an antibiotic or a viral or bacterial infection precipitated the disease or perhaps the sore throat was just a part of the disease. Frequent upper respiratory tract infections were found in association with systemic lupus erythematosus in a study by Nived (1985)[34].

Arthritis was the commonest feature in this series of patients involving mostly the peripheral joints especially those of the hands. One patient who complained of persistant pain in the knee was found to have an avascular necrosis in the articular surface of the medial femoral condyle. Aseptic necrosis was described by Smith (1976)[35] as having a predelection for young people with systemic lupus. This particular patient was aged 21 years and had been on steroids for a period of about one year. The relationship to the corticosteroid therapy was uncertain but it is a well known complication (Abeles 1978[36]).

Cerebral symptoms in systemic lupus have been well described elsewhere[37]. In this series cerebral symptoms from persistant headaches, depression, epilepsy to frank psychosis were seen in 17 patients. Psychosis seen was in the form of puerperal psychosis, abnomal behaviour before the diagnosis and during flare ups of the disease and in one case (case 1.4) It appeared in a patient who had been on steroid maintainance therapy. It was not possible to determine whether this was due to systemic lupus eythematosus or whether it was steroid induced. The patients with depression required antidepressant therapy. Epilepsy occurred in two patients and in both of them it preceeded the other features of systemic lupus by 2 and 7 years. It is interesting that Wilson in Jamaica[24] saw 5 patients who had previously been admitted under psychiatric care who had systemic lupus erythematosus, and in a survey of 350 patients in a mental hospital they found 33% with antinuclear antibodies.

Pleurisy was a complaint in 65% of the patients. It was transient in nature resolving on its own and on occassions was confused with pneumonia. Haemoptysis occurred in several patients and it was generally attributable to lupus pneumonitis. Haemoptysis due to lupus pneumonitis is said to be fairly unusual and seen only in severe systemic disease (Meyers O.L. 1984)[38]. The patients were normally given antibacterial therapy, investigated radiologically and their sputum tested for the presence of acid fast bacilli. Tuberculosis was found once in a patient who had had prednisone for two weeks only suggesting that she probably had the infect-

ion before the treatment.

Seedat (1977)[18] had 3 patients out of his series of 13 who had tuberculosis and he advocated the use of routine isoniazid prophylaxis. This complication was a very rare occurrence amongst the other dermatology patients at Kenyatta National Hospital on long term steroid therapy (Owili)[40].

Evidence of renal involvement was noted in 13 patients with proteinuria and or haematuria and confirmed by renal biopsy in 2 patients. Renal disease did not contribute to any great mortality or morbidity in any of the patients in this series and it was effectively controlled on prednisone alone or in combination with azathiaprime.

Haematological abnormalities seen included thrombocytopenia, leucopenia and anaemia. One patient presented with idiopathic thrombocytopenic purpura for two years before she developed systemic lupus erythematosyis. Karpatkin(1980)[41] found idiopathic thrombocytopaenic purpura to be an early manifestation of systemic lupus,in his patients.The Median time for the development of other symptoms and signs was 3-10 years. Another patient presented with purpura and haemorrhagic bullae; (Tromovitch 1961)[42]. Both these patients initially responded well to prednisone one of them briefly; later succumbing to severe disease with persistant thrombocytopenia which was probably aggravated by azathiaprime which she received as part of her treatment.

A variety of dermatological features (see table 1.4) were observed in these patients. The butterfly rash was seen in only 20% of the patients at presentation in contrast to the 17 (85%) of the patients who eventually developed it over the course of the disease. Case 1.2 had a very unusual presentation. Clinically she had what appeared to be chronic bullous disease of childhood, histologically it was consistant with bullous pemphigoid. She was also on drugs for epilepsy which could have precipitated similar lesions which histologically are difficult to distinguish from those of bullous pemphigoid. It was almost two years later when she developed a butterfly rash that systemic lupus was suspected and diagnosed. Two other patients had a history of flaccid bullous eruptions at the start of their illness which broke down and left raw areas which healed with postinflammatory hyperpigmentation, without scarring. Bullous eruptions over arthritic knees and albows was described by two patients. These and other bullous reactions in systemic lupus have been reviewed by Woodley et al 1985[43] and Hall RP 1982[44]. Antibasement membrane zone antibodies from these bullae have recently been shown to recognize epidermolysis bullosa aquisita autoantigens[43]. Erythema multiforme with systemic lupus (Rowells syndrome)[45] was seen in one patient. Another had a very rare erythematous eruption presenting in the form of erythema annulare centrifugum.

In five patients the disease was precipitated by pregnancy resulting in fetal wastage in 3 cases and severe maternal disease in one patient. None of these patients had been previously diagnosed as having systemic lupus erythematosus. It is possible that they had had a mild form of the disease which was aggravated by pregnancy. Pregnancy associated lupus erythematosus has been found to increase morbidity in less than 10% of the patients with or without lupus nephritis, but it is associated with a high incidence of small for gestational age babies and fetal wastage.[46, 47,48]. This low morbidity was attributed to close monitoring and drug adjustment during the gestation period. Drug therapy through out pregnancy is advocated[49].

A total of 4(20%) of the patients died during the study period all of them within 3 years (6 months to 3 years) of diagnosis with acute disease. Drowitz (1976)[50] showed the existence of a bimodal mortality pattern - those patients dying early in acute disease and infection and others a majority, who died late usually of renal disease which is normally the main cause of death in western series (Wallace 1981)[51]. All patients with the exception of case 1.1 responded well to steroid therapy and on one occasion high dose intravenous (pulse) therapy was used successfully

(ref. High dose intravenous corticosteroid therapy)[52] Steroid side effects were seen at relatively low maintainance doses (in comparison to doses used in European counter parts (Owili[40]) and on two occasions azathiaprime was used in combination as an adjunct because of its steroid sparing effect. There was only one child in this series. The course of the disease in children is the same as in adults Caiero F et al[53]. This child though she presented in an unusual manner, (with bullous eruptions), had a disease similar to others seen elsewhere.

Discoid Lupus Erythematosus.

Eleven patients were included in this study but despite this small number, this form of lupus erythematosus was seen far more frequently than the systemic form. No patient had disseminated discoid. Lupus erythematosus, the lesions tending to be localised and stable. Scalp and preauricular involvement which is associated with increased conversion to the systemic form was seen frequently. Hughes GRV[54]. One female patient who had been on follow up developed systemic features and she has been included in the systemic lupus erythematosus group. A number of patients had chloroquine therapy which was abandoned in favour of topical steroids for lack of effectiveness. The clinical presentation was as seen elsewhere.

Scleroderma.

13 patients were seen with systemic and localised scleroderma. Three patients had the localised form: one girl aged 18 years with linear morphear and the other two patients, both females, with multiple plaque morphea were aged 26 and 8 years respectively. The other 10 fulfilled the American Rheumatism Association's Diagnostic, and Therapeutic Criteria Committees (see appendix III) criteria for the diagnosis of systemic scleroderma.

Elsewhere in Africa a total of 13 patients have been reported with systemic sclerosis, 6 by Basset 1969[13] and the others by Jackyk 1979[14] one of whom he saw himself and the other six from a review of other African cases. Morphea was reported in 4 patients by Basset.

This series of patients presented at Kenyatta National Hospital in the last three years, 6 of them within one year - a higher number than recorded elsewhere in Africa. Jackyks' and Bassets combined series is spread over 13 years.In Tuffanelli's series the annual incidence was 41 new cases per year from 1935 to 1958, all seen at the Mayo clinic.[56] Negroes were said to constitute 38% of all patients with systemic sclerosis (Masi, D'Angelo 1967)[57], with female Blacks having an incidence of 3 times that of White females.

In the clinical manifestations of systemic sclerosis, nonspecific symptoms, weight loss and weakness

Table 6.2. A comparison of clinical features

	This series 10.	Tuffanelli DL[56] 727.	Basset[13] Jackyk[14]
Age range	11-55 yrs	5-86 yrs	10-53
mean	41	41 yrs	-
Sex F-M ratio	2.9-1	3.2	8.5
Cutaneous signs			
sclerosis	10(100%)	100%	13(100%)
fingertip ulceration	5(50%)	35.4%	1
Hyper pigmentation	8(80%)	30.5%	6 (Basset)
swelling preceding sclerosis	4(40%)	23.9%	6* (Basset)
Raynauds phenomena	10(100%)	90	1* (Jackyk)
Gut involvement	7/7(100%)	66%	7 (54%)
Lung involvement	6/8(75%)	27%	3* Jackyk.

* denotes the feature in other cases in that group was not specified.

were seen. Weight loss occurred in 5 patients and weakness was related to myopathy. The skin was involved in all the patients; 5 patients started initially with swelling of the fingers spreading to involve the face and trunk before sclerosis was evident. This presentation is similar to that described by Basset . In comparison all his patients had oedema initially, four starting from the face, 2 from the hands, spreading to involve the trunk, following the classic sequence of oedema, sclerosis and atrophy.

8 patients in this series had a background of diffusely increased pigmentation - a feature also noted by Basset and Jackyk in their patients. Jackyk's patient however is reported as being darkly pigmented without specifying the original complexion. In the other cases it was not specified whether this was a feature or note. Diffuse increase in pigmentation was a presenting feature in two patients before any of the other features became apparent. Other pigmentary dhanges consisted of mottled hypopigmentation (Poikiloderma). This occurred in 7 patients, in 3 involved the face (one the whole face and on the other two it was just evident around the hair line,) and in the others it involved the trunk and the lower limbs. This is a feature which was noted commonly by Tuffanelli whenever there were pigmentary changes in his patients.

All Basset's and Jackyks' patients also had this "spotted achromia" which is a striking features on a Black skin. Calcinosis, a feature seen in the CREST syndrome first described by Tuffanelli and Winkelman 1962[58] was demonstrated on an Xray of the hands on Jackyk's patient. She had all the other criteria for the CREST syndrome except talangiectasis. None of the patients in this series was found to have calcinosis. Raynaud phenomenon was seen in all the patients in this series. Basset makes no mention of it occurring in his patients. It was a presenting feature in (75%) 7 patients as compared to 46% of Tuffanellis' patients. The period between its onset and sclerosis ranged from a few months to two years.

Alopecia is a late sign in systemic sclerosis[55,56] but of some of the patients showed some degree of thinning of the hair, as sclerosis spread to involve the scalp including one patient who presented with "alopecia areata" as a presenting complaint. Neither Basset nor Jackyk made any mention of this feature. One interesting presentation was that of a hemifacial atrophy (see plate 4.) in a female patient but without the ipsilatereal limb wasting of the Parry-Romberge syndrome[59]. The linear morphea seen in one of the patient with morphea started in mid forearm, spread both proximally and distally and caused a contracture deformity in one finger and limitation of movement in the elbow. This lesion evolved to its present

state over a period of 10 years. Linear morphea is reportedly rare in Blacks[55]. Plaque morphea is known to occur in 15% of all childhood scleroderma (Ansell 1976[60]). It was the form seen in the only child presenting with scleroderma. It started from mid thigh on the right leg one year ago and now she has extensive involvement of the trunk and the upper limbs. Basset saw two cases with morphea "en plaque", one possible guttate morphea which was not distinguished from guttate lichen planus and a man of mixed race with the "coup de sabre" variety.

Systemic involvement was demonstrable in 9 out of 10 patients. All Jackyks' patients also had systemic involvement but those reported by Basset were conspiciously devoid of systemic involvement with the exception of one patient (and he emphasised this,) but notably all had severe myopathy. Seven patients in this series had evidence of gastrointestinal involvement. Two patients also had small intestinal involvement one with duodenal diverticular reported before by Queloz J.M. 1972[61]. The other patient had malabsorption with gross abdominal gasseous distension, chronic diarrhoea and wasting. She responded poorly to antibiotics and vitamin supplimments. She presented with symptoms of malabsorption, the skin changes being very subtle were noticed 9 months after she was first seen at the medical out patient clinic. She probably represents the other end of the spectrum where systemic features are pre-

dominant over the cutaneous changes. Malabsorption in systemic sclerosis has been shown to be due to ileal distension with stasis and bacterical overgrowth and not due to permeability disorders (Cobden I et al 1980)[62].

Pulmonary involvement was demonstrated in 6 out of the 8 chest xray examined, and they were seen to show features of various degrees of lung fibrosis. Else where approximately 40% of patients present with radiologically demonstrable lung disease while 70% have abnormal lung function tests[53] (Weaver 1968)[63]. Rowell (1985[64] found lung involvement evident in chest Xrays in 46% of 73 patients examined radiologically in his series.

Five patients had evidence of myopathy clinically and confirmed by needle electromyography out of the seven tested. None of the patients were so severely involved as to be bed-ridden as was the case with Basset's patients. Two of the patients had marked myopathy with atrophy, two had a mild early myopathy and the fifth showed a very interesting variation of myopathic changes only demonstrable in muscles underlying a sclerotic patch, a feature Basset noted in one of his patients. In general muscle involvement is subtle, electromyographic studies may be abnormal and histological changes observable in 40% of patients[65, 55]. Bassets' patient differ in this respect in that the myopathy he observed was severe and his patients were bed ridden with painful atrophic myopathy. In one of his patient he was able to demonstrate anti muscle antibodies.

Cardiac involvement in systemic sclerosis has been well documented (Leroy 1984)[66, 55]. Evidence of cardiac involvement was seen in two patients. One had a large heart and a pericardial effusion demonstrated on echocardiogram and he finally succumbed with congestive cardiac failure. Tuffanelli saw 21 cases with congestive cardiac failure and many others with non specific cardiac changes. The other patient had an abnormal ECG (see plate[12]

No patient had evidence of renal involvement or hypertension. Renal involvement with hypertension occurrs in 8.3 - 12.3% of scleroderma patients (Traub YM et al 1983)[67] and it is a major contributor to acute mortality. 41 patients out of 153 seen by Rowell[64] had some degree of impairment of renal function and the progression of renal disease in males tended to be much greater than in females. Factors predicting the development of renal involvement are discussed by Steen VD et al(1984)[68], frequently there are minor histological changes but only a minority of patients present clinically.[68]

A few of the patients were tried on a course of steroids without a dramatic effect on the clinical status. Routinely they were given Nicotinic acid which subjectively gave them some degree of well being and the ulcers healed although in general it has no place in the management of Raynauds phenomenon[69] having

been surpassed by its analogue nifedipine which has been shown to effect healing of ulcers, but whose long term effect is uncertain (Connally 1984)[70]. Steroids do not affect visceral involvement but are used in inflammatory myositis (Connally)[70] and captopril has been shown to be effective in aborting renal crisis (Connally Backett Brennan 1985)[70,71] The patients were routinely advised to observe general measures like keeping their hands warm.

Only one patient is known to have died in this series. In Tuffanelli's series 29.7% died within five years giving him a five year servival rate of 70.3% Nine of his patients underwent complete clinical resolution. Medsgar J.A. et al (1971)[72] in a retrospective analysis of clinical and demographic factors, found a significant correllation between mortality, increasing age, internal organ in involvement (particularly cardiac and renal) and steroid therapy. Prognosis was worse in males than in females and the survival from the time of diagnosis to death, was shorter in the Negro. Survival figures in children are similar to those in adults.(Ansell B.M.)[60] None of the environmental factors which cause scleroderma-like changes (Haustein UF 1985)[80] e.g. mining, contact with polyvinyl chloride, silica were associated with the patients in this series.

Dermatomyositis.

The 3 patients with dermatomyositis were each in the definite, probable and possible classes. The patients with the definite and probable diagnosis presented classically with the classical myopathy and cutaneous changes [31]. The patient with the probable diagnosis would probably have been definite and it has been possible to do all the investigations.

An unusual finding was the presentation of hoarseness of voice seven years before the development of other features leading to the suspicion of and diagnosis of dermatomyositis. Whereas laryngeal disturbances are part and parcel of the disease, they normally occur with the myopathy.[31] This hoarseness of voice eventually responded to steroid therapy.

The second patient presented with a short history - less than one year but when he was first seen he already had begun to show signs of muscle atrophy which normally occurrs long after the onset of myopathy (Bohan & Peters 1975)[73]. He also had a persistent bradycardia (see plate). Rhythm disturbances in dermatomyositis have been well described by Fernandes 1971)[74]. Haupt HM et al (1982) [32] found that out of 16 autopsied cases of patients with cardiac involvement two who had had bundle branch block had direct involvement of conduction system with contraband necrosis. Seven who

had had congestive cardiac failure had microscopic evidence of myocarditis and focal myocardial fibrosis.

Dermatomyositis presents at one end with predominantly dermatological changes and at the other with myopathic changes.[31] The third patient fell in to the other side of the spectrum. He had edema and infiltration periorbitally and facially for three years without noticeable myopathy. Diagnosis was reached on biopsy after length investigations.

Association of cancer with dermatomyositis is recognised in 15 - 34% of patients, Vanderploeg DE 1977, Bohan Peters (1977)[75 76] and it is recommended that patients should be screened for cancer. None of these three patients showed any evidence of malignancy.

The first two patients were treated with steroids with good response. A review of the remission rate in 289 treated and untreated patients by Winkelman et al (1968)[77] showed that almost 50% of the remission occurred spontaneously but that steroids contributed to a reduced morbidity and a faster rate of achievement of remission and he made the suggestion that steroids should be given in an initial high dosage and reduced to a low maintainance dose. These two patients are on a maintainance dose of 5mg prednisone daily and doing very well. A repeat electromyograph on one of the cases showed a reversion to almost normal readings.

Other forms of therapy have been used like plasma-pharesis with significant reduction in histological changes (Benningtom JL et al 1981)[78].

Dermatomyositis has not been described in Africans in major journals in the last fifteen years although it is readily seen elsewhere (Medsgar TAJ et al)[79].

Antinuclear antibody immune complexes, complement and immunoglobulin profiles.

Antinuclear antibodies were tested for in 77 patients and 57 controls. Out of these 20(100%) of systemic lupus erythematosus were positive as were 3(23.1%) with scleroderma, 1 dermatomyositis, 4(16.6%) rheumatoids arthritis and 4 others with ill defined connective tissue disease entities. 2(3.5%) out of 57 controls were also positive. Notably in this series none of the 11 discoid lupus patients were positive. The demonstration of LE cell in 14(70%) of our systemic lupus erythematosus patients correlated well with others - 61% found in the Jamaica series, which was a series consisting predominantly of Black patients (93 Black and 2 Chinese) (Wilson 1979)[20] 85% (Grigor et al 1978)[85] 69% (Lee et al 1978)[87]. As antinuclear antibody testing by indirect immunofluorescence has largely superceeded the LE cell demonstration where immunology facilities are not available the latter is a useful test. It's disadvantage lies in the fact that it only represents certain antibodies directed against DNA - histone complex (Nisengard)[82].

The antinuclear antibody positivity was significantly higher in the combined connective tissue group as compared to the control group. Antinuclear antibody

positivity is dependent on a number of variables and may vary from laboratory to laboratory. In this study the substrate used was cryostat sections of rat liver. This gives totally different result when compared to Hep - 2 cell lines, which give quantitatively and qualitatively better readings (Bernstein and Hughes)[87]. Some of the disorders also show substrate specificity. Scleroderma in one series (Jablonsky S, Chorleski)[82] demonstrated a substrate specificity of 49% with a positivity rate of 62% on rat liver as compared to 97% on monkey eosophagus. In our series the demonstration of antinuclear antibody in scleroderma was relatively low (23%) on rat liver substrate. Relative disease activity can affect the positivity of antinuclear antibodies. Whereas this is not a marked phenomenon in systemic lupus erythematosus, serial evaluation of sera from scleroderma patients increase the positivity rates. In this series antinucleas antibody test was done only once. Only single evaluations were done in these patients.

Because of the lack of standardisation individual laboratories must enumerate their own normal values. A positive reading at a dilution of 1 in 10 was considered significant. At this dilution only 3.7% of the controls were positive. This is supported by an earlier observation (Bowry T et al 1984)[88] who found 1.0%(1 out of 99) positivity rate

at this dilution, in 99 hospital based patients.

The significance of the antinuclear antibodies.

All the patients with systemic lupus erythematosus had positive antinuclear antibody and this signifies it's diagnostic importance. It would seem that when one compares this to other series ref. Nisengard[82] that using a comparable substrate, antinuclear antibody titres are lower in our laboratory, the high titres so often quoted in Western figures not being seen, even in on new and untreated patients. The explanation for this is not obvious but other works with other auto-antibody systems have hinted at a genetic predes-position of Caucasians and Blacks sharing certain HLA haplotypes with Caucasians, to have higher auto antibody titres or presence of certain auto antibodies.[83]

The antinuclear antibody positivity compared with other predominantly black series Wilson[24] had an 84% positivity rate using a calf thymus nuclei as substrate at 1/40 dilution, Lee[86] and Grigor[85] had 88% and 100% antinuclear antibody positivity respectively.

No patient in this series was suspected of having antinuclear antibody negative systemic lupus described elsewhere (Maddison PJ 1984)[88]. Most of our patients when enrolled in study were on treatment and the antibody titres ranged from 1/10 - 1/80, the highest titres occurring relatively more commonly in the untreated group. There was no correlation between the clinical disease activity and the antibody titres, some of the severely ill patients having a low titre while others who were relatively well clinically had high titres. Antibody titres not correllating with treatment were recognised by others (Nisengard[82], Gladman and Urowitz)[90]. 48% - 95% positivity is found in systemic sclerosis (Jablonska Chorlezki)[82] but it relatively infrequently in morphea[82] childhood scleroderma shows similar patterns 0-15 (Ansell)[60], to the adult form and one of the positive sera belonged to a child with plaque morphea. In relation to drugs and drug induced lupus, only two of the patients with systemic lupus and epilepsy had a positive history of drugs ingestion but the sequence of events was not in keeping with the possibility of drug induced lupus syndrome.

The patterns of antinuclear factor seen were humogeneous, granular, speckled, peripheral and nucleolar.

The homogeneous pattern which is related to the presence of anti DNA antibodies, and LE cells in vitro (Nisengard Blockz)[82], was the commonest pattern seen in systemic lupus. The other patterns seen were - the peripheral pattern which is, considered to be the most specific for systemic lupus and associated in 33% with patients with renal involvement and with the demonstration of antidouble stranded DNA in 25%[82].

Speckled pattern which is the pattern most often seen in scleroderma,(80%) and associated with extractable nuclear antigen (Wangle AG[92], Provost)[93] was seen in two patients. Antinucleolar antibody pattern was seen in 2 patients both with scleroderma. This antibody pattern has a high specificity for scleroderma and it occurrs in 16% of these patients and rarely in the other diseases (Jablonska)[82].

Although all the discoid lupus erythematosus patients were seronegative in this study antibodies to nuclear antigens in significant titres are seen, and they have been associated with those patients who tend to convert to the systemic form (Millard et al)[94,81]. In the Rheumatoid arthritis patients antinuclear antibodies were seen in 4(16.6%) of the patients in this series. In the Jamaica series of predominantly Black patients with rheumatoid arthritis Wilson[24] found 26% seropositivity in 115 patients. They are usually associated with juvenile rheumatoid arthritis and two of our patients on whom they were demonstrated were juvenile cases.

Circulating immune complexes, complement consumption and immunoglobulins.

Significant circulating immune complexes of IgG and IgA, lgM classes and complement consumption was demonstrated in the combined connective tissue group Cl_q C_3 C_4 and in systemic lupus erythematosus as compared to the controls.

The difference was more prominent in the systemic lupus group as compared to the combined group and the controls. There was no definite difference between the treated and the untreated. There was a marginal difference in the total lgG level in the systemic lupus group being higher than in the control, but in general total immunoglobulins in controls were not significantly different from those of the patients.

Circulating immune complexes and complement consumption are usually seen in patients with active systemic lupus but may also be seen in systemic scleroderma dermatomyositis and in some instances discoid lupus. Immune complexes, complement consumption in this study was seen mainly in systemic lupus patients but in the other disorders it was only marked in one patient with systemic sclerosis.

In the patients with systemic lupus 4 patients in the untreated group and 3 in the treated group showed low complement consumption of Cl_q, C_3, C_4 and in 5 of these patients this combination was associated

with increase in disease activity or death. One patient stayed relatively well up to the time she was last seen - 3 months later - the other recovered but has residue renal disease. C_3 C_4 combination seen in 1 patient not on treatment and on treatment was also associated with an increase in morbidity in the treated group the untreated patient going on to make a good recovery low complement activity was reflected in low disease activity and good therapeutic control.

In the Jamaica series, Wilson[24] found that low C_3 and C_4 combination correllated well with disease activity, 75% with this combination having renal disease while only 34% had increased clinical activity without renal disease.

Schur PH et al 1981[6] followed up 27 patients with systemic lupus erythematosus over a period of and found that the lowest mean values for Cl_q, C_4, C_3 and CH50 were found in patients with combined renal and non renal flare up.

Low C_3 was found in most patients with renal flare up but only in 39% without renal involvement and thus was a good predictive indicator of active nephritis. Low C_4 predicted general clinical flare up and 25% of those going to have a renal flare up. C_4 was the first complement to return to normal levels after adequate control. Good correllation between disease

activity and immune complexes have been demonstrated by others (Sturfelt G et al 1985)[95].

Monitoring of complement activity during follow up of patients has been advocated by some authors[97] as being useful in the prediction of deterioration of clinical disease and hence early adjustment of treatment and more effective end organ protection. Other authors disagree with this (Hughes GRV)[54] preferring to manage patients judging by their clinical status. In our patients it would seem that this may be useful predictor of morbidity and considering the observation by Owili[40], that in general African dermatological patients in Kenyatta National Hospital, tolerate high doses of steroids poorly with a high incidence of severe side effects, complement assays could be an important. Congenital complement deficiencies in Cl_q, C_3 C_4 C_5 have also been associated with lupus syndromes (Block KJ)[96].

Conclusion.

An unexpected number of patients were seen when one considers reports from elsewhere in Africa. The clinical presentations were similar to those described previously and almost all the patients were seen in the dermatology department.

Patients with systemic lupus appeared to have relatively severe disease perhaps due to the selectivity that results from the referal system practised in the health system. It is possible that the milder cases are filtered before they reach the dermatology or medical clinics so that by the time they are seen there they are fairly ill, alternatively the large number is as a result of the fact that persons with skin lesions are referred to the skin clinic where diagnosis is readily made. Diversity in clinical presentation was marked. Antinuclear antibody positivity in systemic lupus was 100% as compared to the LE cell positivity of 70%. This correllates well with figures given elsewhere so it is still a useful test where immunology laboratory facilities are not available. Although scleroderma does show a high substrate specificity the antinuclear antibody positivity was lower than that expected using rat liver as a substrate.

Demonstration of antinuclear antibody at a 1.10 dilution was found in only 3.5% of healthy controls and at this dilution a positive antinuclear antibody finding was considered significant. The nuclear patterns seen were comparable to those seen elsewhere with the nucleolar pattern demonstrable in scleroderma patients. Antinuclear antibody was considered to be of a high diagnostic value especially in systemic lupus erythematosus. The titres in these patients were considerably lower than in caucasians.

Complement and circulating immune complexes were significantly abnormal in the connective tissue diseases especially in systemic lupus erythematosus, where they were shown to correlate well with the clinical disease activity and to have a predictive value in increased disease activity and thus useful in this respect. Low Cl_q C_3 C_4 combination was especially associated with a high morbidity and mortality. Total immunoglobulin estimations were not found to be of any correlative or predictive value.

There was no malignancy associated dermatomyositis or drug induced lupus erythematosus or environmentally induced scleroderma seen.

The clinical presentation of all the conditions showed a wide variation in clinical presentations.

Appendix 1. Questionnaire.

I Name

Age

Sex

Unit No.

IDH No.

Place of birth

Residence

Date

Occupation

II Diagnosis

Initial presentation of illness·

Onset of illness insidious/acute

Date first seen in hospital..... In K.N.H.

Presenting complaints and their onset and

Duration.....

.....

Enquiry on systems as regards initial presentation of the illness.

General

Central Nervous system

Cardiovascular system

Abdomen

Respiratory system

Genitourinary system

Muskulo skeletal system

Skin

Family history

Past medical history

Drug history

Pregnancy

Psychiatric history

Medical including infections and frequency of infections.

III Symptoms and physical signs when firot seen at K.N.H.

..... Date.....

General

Central Nervous

Cardiovascular

Respiratory

Abdominal

Musculoskeletal

Skin

Management (response to management and subsequent observations till time of presentation.

IV Present symptoms Date.....

General

Central Nervous system

Cardiovascular

Respiratory

Abdominal

Muskulo skeletal

Skin

V Laboratory Examination

1. Blood HB WBC..... Differential count lymphocytes.....

Polymorphs..... Monocytes,eosinophils.....platelets.

ESR

Coombs test

Coagulation screen.

2. Urea and electrolytes

   serum creatinine

3. Liver function test SGOT SGPT $AlkPO_4$
   CPK

   albumin globulin

   Total protein PTI

4. Antinuclear antibodies.....pattern.....Le cells.

   Rheumatoid factor

   Complements

   Cryoglobulins

   Kahn test.

5. Chest xray

   other xrays

   Histological examination

   Special examination e.g. ECG, EMG

   follow up notes.

(Note the questionnaire is scaled down in the space allocated for filling in details).

Appendix II

Systemic Lupus Erythematosus. The 1982 Revised Criteria for the classification of systemic lupus erythematosus. Tan Em Cohen AS Fries et al Arthritis Rheum 1982 25 1271 -7.

Criteria

1. Malar rash - Fixed erythema, flat or raised over the malar prominences, tending to spare the nasolabial folds.

2. Discoid rash - Erythematous raised patches with adherent keratotic scalling and follicular plugging, atrophic scarring may occur in older lesions.

3. Photosensitivity - Rash as a result of unusual reaction to sunlight by history or physician observation.

4. Oral ulcers Oral or nasopharyngeal ulceration usually painless, observed by a physician.

5. Arthritis Non erosive arthritis involving 2 or more peripheral joints, characterised by tenderness, swelling or effusion.

6. Serositis Pleuritis convincing history of pleuritic pain or rub heard by a physician or evidence of pleural

		effusion or (2) pericarditis documented by ECG or rub or evidence of pericardial effusion.
7.	Renal disorder	Persistant proteinuria $>$ 0.5g/d or 3+ if quantitation not performed or (2) cellular casts may be haemoglobin, granular, hyaline or mixed.
8.	Neurological disorders	Seizures in abscence of offending drugs or known metabolic derangements e.g. uraemia, ketoacidosis or electrolyte imbalance or (2) psychosis in absence of offending drugs or known metabolic derangements e.g. uraemia, ketoacidosis or electrolyte imbalance.
9.	Haematological disorder	Haemolytic anaemia with reticulo cytosis or (2) leukopaenia 4000/cumm total on 2 or more occasions or (3) lymphopenia 1,500/cumm on 2 or more occasions or (4) thrombocytopenia 100,000/cumm in the absence of offending drugs.

10.	Immunological disorder	(1) Positive LE cell or (2) DNA antibodies in abnormal titres or (3) the presence of antibody to the SM nuclear antgen or (4) false the serologic test for syphillis for over 6 months.
11.	Antinuclear antibodies	abnormal titre of antinuclear antibody by IF or an equivalent assay at any point in time and in absence of drugs known to be associated with drug induced LE syndrome.

A person shall be said to have SLE if any 4 or more of 11 criteria are present serially or simultaneously, during any interval of observation.

Appendix III: Scleroderma.

Criteria for diagnosis of systemic sclerosis

"Preliminary criteria for systemic sclerosis
1980 subcommittee for scleroderma criteria
of the American Rheumatism Associations.
Diagnostic and Therapeutic criteria
Committee 1980: Arthritis and Rheumatism
23, 581"

Sole major criterion	-	Proximal scleroderma
or		
Two or more minor	-	Sclerodactaly
criteria	-	Digital pitted scars of finger tips or loss distal finger pad.
	-	bilateral basilar pulmonary fibrosis

APPENDIX IV: Dermatomyositis
criteria for diagnosis.

DERMATOMYOSITIS

Bohan A., Peter J.B. 1975, Polymyositis and Dermatomyositis N. Eng. J. Med. 292: 341 - 347, 403 - 407.

1. Symmetrical and progressive weakness of muscles in the limbs and girdle; sometimes also involvement of the muscles of breathing or swallowing.

2. Muscle biopsy showing necrosis of muscle bundles with phagocytosis, regeneration with basophilia, and inflammatory exudate.

3. Increase in muscle creatinine phosphokinase and aldolase.

4. Abnormal electromyogram with short, small polyphasic motor units, fibrillations, bizarre high frequency discharges.

5. Dermatological features, most notably neliotrope eye and Gottron's papules.

Criteria required to make:-

a) Definite diagnosis - four
b) Probable diagnosis - two - three
c) Possible diagnosis - one - two.

APPENDIX V

Classification of Rheumatoid Arthritis

Rope et al. 1958, Revision of diagnostic criteria for rheumatoid arthritis. Bull Rheum. Dis. 1958; 9: 175-176. The ARA criteria for diagnosis of rheumatoid arthritis.

1. morning stiffness
2. pain on motion or tenderness at least one joint
3. swelling of at least one joint
4. swelling of at least one other joint within 3 months
5. symmetrical joint swelling
6. subcutaneous nodules
7. Xray changes typical of R.A.
8. Positive agglutination test
9. poor mucin precipitate from synovial fluid
10. Characteristic histological changes in synovial membrane
11. characteristic histological changes in nodules.

Classification of rheumatoid arthritis based on ARA criteria.

1. classic rheumatoid arthritis seven ARA criteria fulfilled articular symptoms present for at least 6 weeks.

2. Definite Rh. arthritis 5 ARA criteria, articular symptoms present for at least 6 weeks.
3. Probable rheumatoid arthritis. 3 ARA criteria fulfilled articular symptoms present for at least 4 weeks.
4. Possible rheumatoid arthritis 2 ARA criteria fulfilled; articular symptoms present for at least 3 weeks.

(5)

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