POLYARTHRITIS IN WESTERN NIGERIA

II. STILL'S DISEASE

BY

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This paper describes the clinical features of 29 Nigerian children with polyarthritis who satisfied the criteria for a diagnosis of Still's disease (Ansell and Bywaters, 1959). These patients were seen during the course of a survey into the pattern of polyarthritis occurring at University College Hospital (U.C.H.), Ibadan, Nigeria. The methods employed in this survey have been previously described (Greenwood, 1969); 24 of the children had been admitted to this hospital during the years 1957 to 1967, and the remainder presented at the out-patients department during the years 1965 to 1967.

Patients

Fourteen of the 29 children studied were male and fifteen female. The age at the onset of symptoms varied from 18 months to 15 years (Fig. 1). The maximum incidence occurred in children in the age groups 0 to 3 and 13 to 15 years old.

Fig. 1.—Distribution of age at onset in 29 Nigerian children with Still's disease.

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Clinical Findings

Of the 29 patients 28 presented with joint pain or swelling and ten presented with an additional history of fever. Other symptoms were uncommon. The duration of symptoms varied from 2 weeks to 3 years (mean 1.3 years) at the time of presentation. Many of the patients with longer histories had received some form of treatment at a local government hospital before presenting at U.C.H., Ibadan.

Arthritis

There were signs of polyarthritis in 28 of the 29 patients at the time of presentation. No example of mono-articular involvement was encountered. The arthritis was predominantly symmetrical with frequent involvement of the ankles, knees, and wrists (Table I).

TABLE I
SITE OF JOINT INVOLVEMENT IN 29 NIGERIAN CHILDREN WITH STILL'S DISEASE

Joint	Number of patients with involvement of the joint
Ankles	24
Knees	20
Wrists	17
Elbows	12
Metacarpophalangeal	9
Proximal interphalangeal	7
Cervical spine	7
Hips	5
Metatarsophalangeal	5
Temporomandibular	2
Shoulders	2

Fever

Pyrexia was observed in fifteen of the 24 patients admitted to hospital but this was rarely marked. Only two patients showed daily temperature swings of more than 2°F. and one of these children had associated tuberculosis.

Rash

This was noted in seven patients. This was probably coincidental in a child with a pustular eruption and in another child with a generalized vesicular eruption. The remaining five patients had a macular rash, maximal on

the trunk, which was typical of the rash of Still's disease. In one patient marked fluctuation in the intensity of the rash was observed from day to day. The rash was seen best in patients with a paler skin, but was readily discernible in spite of skin pigmentation. The lesions, which were coloured more darkly than the surrounding skin, were larger than those usually seen in English patients and tended to become confluent.

Other symptoms and signs

Generalized lymphadenopathy was noted in twelve patients. Enlarged fluctuant cervical glands found in another child were probably tuberculous. The spleen was enlarged one finger's breadth or more below the costal margin in eleven children. Iritis was not seen but slit-lamp examination was not performed routinely. Chronic conjunctivitis and corneal scarring in one patient were probably sequelae of an attack of smallpox 6 years previously. None of the patients had any clinical features of pericarditis. However, generalized enlargement of the cardiac contour, noted on the chest x ray of three children who had no other features of cardiac disease, was probably due to a pericardial effusion. One of seven electrocardiograms showed T-wave changes consistent with a diagnosis of pericarditis.

Haematological Findings

The haemoglobin values found at the time of presentation in the 29 children with Still's disease are compared with values obtained in healthy Nigerian children under the age of 16 years old in Fig. 2. The children with Still's disease were found to have a significantly lower mean haemoglobin level than the healthy children (10.4 compared with 11.1 g./100 ml.) but the difference is not marked. Most of the patients and controls were anaemic by European standards.

Fig. 2.—Distribution of haemoglobin levels in 29 Nigerian children with Still's disease and in fifty healthy controls.

The white cell count at the time of presentation varied from 2,600 to 16,000/cu. mm. (mean 7,650). A white cell count of 30,000/cu. mm. was obtained during the course of the illness of a 6-year-old girl in whom a diagnosis of leukaemia was suspected as she had no articular features of Still's disease at this time. Two of the six

patients with white cell counts of over 10,000/cu. mm. had a marked eosinophilia which was probably related to an associated helminth infection. In the remaining patients with a leucocytosis, polymorphonuclear leucocytes predominated.

A raised erythrocyte sedimentation rate was found in 23 of the 24 patients in whom the investigation was carried out. Elevation of the erythrocyte sedimentation rate is, however, a common finding in apparently healthy Nigerian children.

The distribution of the genotype in the 26 patients in whom the investigation was performed (AA in 14, AS in 10, and AC in 2) shows no significant difference from the pattern seen in children admitted to U.C.H., Ibadan, with other general medical conditions.

Immunological Findings

None of the eight patients tested on presentation gave a positive test for rheumatoid factor. However, at follow-up examination 2 years after presentation, a 14-year-old girl had become positive to both the latex-fixation and the human erythrocyte agglutination tests.

Plasma protein electrophoresis was performed in nineteen children. In all patients a variable degree of elevation of the γ -globulin was seen, and in one child marked elevation of the α_2 globulin was also noted.

Immunoglobulin levels were assayed by the method of Fahey and McKelvey (1965) in fourteen of the children with Still's disease and in 34 healthy Nigerian children. A wide range of scatter was observed in each group but the mean values for the children with Still's disease did not differ significantly from the mean values obtained in the controls (Table II). The higher mean level of IgA obtained in the patients with Still's disease was largely accounted for by the findings in a severely disabled 17-year-old girl who had an IgA level of 500 per cent. of the M.R.C. standard. Mean IgG and IgM levels were high in both patients and controls.

TABLE II
MEAN IMMUNOGLOBULIN LEVELS IN HEALTHY CHILDREN AND THOSE WITH STILL'S DISEASE
VALUES EXPRESSED AS A PERCENTAGE OF THE
M.R.C. IMMUNOGLOBULIN STANDARD

Immunoglobulin	Children with Still's Disease (14)	Healthy Children (34)
IgA	130 ± 110	70 ± 40
IgG	260 ± 90	250 ± 115
IgM	260 ± 140	310 ± 210

Synovial Fluid and Synovial Biopsies

Synovial fluid was obtained from seven children. In each sample elevation of the protein content was observed with a mean of 5 g./100 ml. The total cell counts varied from 3,000 to 30,000/cu. mm. Polymorphonuclear leucocytes predominated in each sample.

Synovial biopsies were taken from five patients. In four specimens synovial hyperplasia was present. Cellular infiltration with lymphocytes, plasma cells, and polymorphonuclear leucocytes were present in each

biopsy, but the relative proportions of these cell types varied from specimen to specimen (Fig. 3.) Small aggregates of lymphocytes were present in one biopsy but no true follicles were observed. Increased vascularity of the synovium was a prominent feature in each case but no abnormal changes were seen in the vessel walls.

Radiological Findings

Abnormal radiological appearances were observed in the *x* rays of fourteen of the 29 patients (Table III) and were seen frequently in the large joints. Three children had radiological signs of severe disease at the hips with erosions, loss of joint space, and in one case protrusio acetabuli. Bilateral sacroiliitis was noted in only one of the thirteen pelvic *x* rays taken. Changes at the knee were less severe but loss of joint space and erosions were noted in four patients.

Review of the thirteen abnormal hand *x* rays showed that the brunt of the disease had fallen on the bones of the carpus. Loss of joint space was observed more frequently in the carpus than at the finger joints. The distribution of erosions showed a similar predilection for the carpus (Fig. 4, overleaf). Large erosions of the

TABLE III
RADIOLOGICAL FINDINGS IN 29 NIGERIAN
CHILDREN WITH STILL'S DISEASE

Site of <i>x</i> ray	Number of Patients <i>x</i> -rayed	Number of Abnormal Films
Hands	28	12
Feet	26	3
Knees	26	4
Pelvis	13	4
Cervical spine	8	2
Ankles	5	1
Elbows	3	0
Chest	21	5

scaphoid bone, of the type seen frequently in adult Nigerian patients with rheumatoid arthritis, were observed in two patients. Growth defects were present in seven hand *x* rays, involving particularly the proximal phalanges, which were shortened or abnormally wide. Radiological changes occurred less frequently in the feet than in the hands and only three abnormal *x* rays of the feet were seen. In each of these films erosions were present at the metatarsophalangeal joints and in two instances these were accompanied by subluxations.

An increase in the cardiac contour was noted in five of the 21 chest *x* rays taken. One of these children had

Fig. 3.—Synovial biopsy from the knee of an 11-year-old Nigerian boy with Still's disease, showing infiltration of the synovium with lymphocytes and plasma cells. $\times 150$.

Fig. 4.—Hand x-ray of a 14-year-old Nigerian girl, showing the typical changes of severe Still's disease.

congenital heart disease and another had rheumatic mitral valve disease. None of the remaining three patients had any clinical features of heart disease and the increased cardiac shadow was probably due to a pericardial effusion. In one child return of the cardiac size to normal was observed in a further chest x ray taken 6 months after the cardiac enlargement had been first detected.

Treatment

Symptomatic treatment with salicylates was employed in all patients. Satisfactory analgesia was achieved but difficulty was experienced in assessing dosage for small children as facilities were not available for determination of blood salicylate levels. Five children were given a short course of steroid therapy whilst in hospital but in each child the drug was withdrawn at a later stage and none of them received a prolonged course. Considerable difficulty was encountered in the management of children with joint deformity. Whilst the children

were in hospital some degree of correction was obtained by serial splinting and daily physiotherapy, but long periods of hospital admission were not practicable. Regular out-patient therapy was difficult to arrange, as many patients could not afford the cost of transport to and from hospital.

Prognosis

An 18-month-old baby contracted measles whilst in the ward and died of fulminating bronchopneumonia, in spite of massive antibiotic therapy. Nineteen of the remaining patients were traced and examined a few months to 9 years after the onset of their illness. At follow-up examination it was found that most of the children had improved sufficiently to live a normal life, but that many had been left with some joint residua. Examination with portable x-ray apparatus showed that in two cases radiological erosions had healed without any treatment in the period between presentation and follow-up. The number of children showing improvement at follow-up was greater among patients seen for the first time within one year of the onset of their disease than in those with longer histories at the time of presentation.

The findings of thirteen patients followed for more than 1 year, with a mean duration of follow-up of 4.3 years, are compared with the results obtained at a 5-year follow-up of 116 English patients with Still's disease using the same criteria (Ansell and Bywaters, 1959 (Table IV)). There is little difference in the functional status at follow-up, but joint residua were found more frequently in the Nigerian children and fewer Nigerian children were thought to have improved.

TABLE IV
COMPARISON OF THE FOLLOW-UP FINDINGS IN
116 ENGLISH CHILDREN AND 13 NIGERIAN
CHILDREN WITH STILL'S DISEASE
BASED ON DATA OF ANSELL AND BYWATERS
(1959)

Series	English	Nigerian
Number of cases	116	13
Mean duration of follow-up (yrs)	5	4.3
Functional Status 4 and 5 (per cent.)	78	77 (10)
Absence of joint residua (per cent.)	27	15 (2)
Inactive disease (per cent.)	53	54 (7)
Clinical improvement (per cent.)	94	54 (7)
Mean change in functional status from time of presentation	2.5 to 4.7	2.7 to 4.0

Discussion

The occurrence of Still's disease in tropical Africa has been previously noted on a few occasions. Dubois, Guérineau, Cayret, Grelrier, and Ravix (1963) reported three cases of the disease seen in Senegal. Hijmans, Valkenburg, Muller, and Grattama (1964) included the case of a child aged 13

in their series of three patients with rheumatoid arthritis seen in Liberia. Hall's series of 106 Kenyan patients with polyarthritis included one case of Still's disease (Hall, 1966). The occurrence of juvenile rheumatoid arthritis at U.C.H., Ibadan, Nigeria, has been previously reported by Anumonye (1964). Two of the four patients described in his report have been included in the present study.

The prevalence rate of Still's disease in temperate climates is not accurately known, but it is probably an uncommon condition. The incidence of the disease in children living in the neighbourhood of the M.R.C. Rheumatism Research Unit, Taplow, has been estimated at 0.06 per cent. (Bywaters, 1968). In temperate climates the prevalence of Still's disease is much lower than that of adult rheumatoid arthritis. At the M.R.C. Rheumatism Research Unit, Taplow, which has a special interest in the treatment of Still's disease, new cases of adult rheumatoid arthritis are seen ten to 20 times more frequently than cases of Still's disease. Approximately twelve new cases of Still's disease are seen in this unit each year.

The presentation of ten new cases of Still's disease at U.C.H., Ibadan, during a 2-year period suggests that the incidence of the disease in Western Nigeria is comparable to that observed in temperate climates. At U.C.H., Ibadan, Still's disease was found to account for half as many hospital admissions as adult rheumatoid arthritis, a much higher proportion than that observed in temperate climates. This difference appears to be too marked to be dependent solely upon the relatively large proportion of the Nigerian population under the age of 16 years and suggests a high prevalence rate for Still's disease or a low prevalence rate for adult rheumatoid arthritis in this community. There is evidence that the latter is the important factor (Greenwood, 1968).

Review of the clinical characteristics of Nigerian children with Still's disease showed that these followed closely the pattern of the disease described in European children. Two peaks of maximum incidence were found, in the age group 1 to 3 years old and at puberty, as noted previously in English children (Ansell, 1965). The distribution of the arthritis paralleled that described in European children. Involvement of the hips and knees was seen more frequently than in adult Nigerian patients with rheumatoid arthritis. Monoarticular involvement was not seen. This may be partly due to the long period that had elapsed in most cases between the onset of the disease and presentation at U.C.H., Ibadan, but probably also indicates the greater

tendency of patients with polyarticular involvement to seek specialist treatment.

Only two examples were seen of the widely swinging daily temperature noted by McMinn and Bywaters (1959) and one of these children had associated tuberculosis. However, a milder degree of fever was seen commonly in patients admitted to hospital. Splenomegaly was frequent but this finding is of little significance in a community where malaria is endemic. The characteristic rash of Still's disease (Isdale and Bywaters, 1956) was seen in five children and mild lesions may have been obscured in other patients by skin pigmentation. Four of the five children with an obvious rash had features of visceral involvement, an association noted by Isdale and Bywaters (1956). None of the Nigerian children had any clinical features of pericarditis, noted in 7 per cent. of English children with the disease by Lietman and Bywaters (1963), but three children showed radiological and cardiographic features consistent with the presence of a pericardial effusion. Iritis and subcutaneous nodules were not seen.

Polymorphoneutrophil leucocytosis, shown by Schlesinger and Cathie (1951) to be a common feature of the disease, was noted in several children. The low incidence of rheumatoid factor (5 per cent.) corresponds to the findings in English children (Bywaters, Carter, and Scott, 1959). No significant difference was found between the mean immunoglobulin levels of Nigerian children with Still's disease and healthy Nigerian children. In both groups, mean IgG and IgM levels were raised by European standards. Elevation of IgG and IgM levels in children living in the Gambia has been previously noted by Rowe, McGregor, Smith, Hall, and Williams (1968).

The histology of synovial biopsies obtained from several cases was characteristic of the disease. Typical x-ray changes of Still's disease were seen in the hands, feet, hips, and knees. In contrast to the findings in adult Nigerian patients with rheumatoid arthritis, radiological changes were often severe. Radiological involvement of the sacroiliac joints was seen less frequently than the 23.7 per cent. noted in English children by Carter (1962). This finding is of interest in view of the rarity of ankylosing spondylitis in Nigerians and the low incidence of sacroiliitis seen in Nigerian patients with Reiter's syndrome.

Comparison of the clinical status of Nigerian and English children with Still's disease followed for a 5-year period showed that Nigerian children did not do as well as their English counterparts. The

difference is, however, not marked and the percentage of children in functional states 4 and 5 at the 5-year follow-up is identical in each series. The slightly poorer prognosis in Nigerian children with the condition can be attributed to the fact that few had received more than a few months of treatment.

The prevalence of Still's disease in Nigerian children appears to be comparable to that observed in temperate climates, and the clinical features of Nigerian children with the condition correspond closely to those seen in European children. These findings are of interest in relation to the infrequent occurrence of adult rheumatoid arthritis in the same population and the unusual features observed in adult Nigerian patients with polyarthritis who satisfied the American Rheumatism Association criteria for a diagnosis of definite or probable rheumatoid arthritis. These observations support the view that Still's disease in children and rheumatoid arthritis in adults are distinct clinical entities.

Summary

The clinical features are reported of 29 Nigerian children with Still's disease studied during an

investigation into the pattern of polyarthritis seen among patients presenting at University College Hospital, Ibadan. The clinical, radiological, and laboratory findings closely resemble those reported in European children. This is of interest in contrast to the comparative rarity of the adult form of rheumatoid arthritis in the same community.

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La polyarthrite en Nigérie Occidentale
II. La maladie de Still

RÉSUMÉ

Les signes cliniques sont rapportés chez 29 enfants nigériens atteints de la maladie de Still qui ont été étudiés pendant un relevé des différents genres de polyarthrite parmi les malades se présentant à University College Hospital, à Ibadan. Les constatations cliniques, radiologiques et de laboratoire ressemblent de près à celles rapportées chez les enfants européens. Cela est d'intérêt en contraste à la rareté comparative de la forme adulte de la polyarthrite rhumatoïde dans la même communauté.

Poliarthritis en Nigeria Occidental
II. Enfermedad de Still

SUMARIO

Se exponen las características clínicas de 29 niños nigerianos con síndrome de Still, examinados durante una investigación sobre el esquema de la poliartrosis entre pacientes del University College Hospital, en Ibadán. Los resultados clínicos, radiológicos y de laboratorio se asemejan en gran medida a aquellos hallados en niños europeos con la misma enfermedad. Esto es interesante, en contraste con los casos, comparativamente raros, de adultos con poliartrosis reumatoide en la misma comunidad.