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Burkitt's Lymphoma in Children at Ibadan: a review of 133 cases

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Summary

Aderele, W. I. and Antia, A. U. (1979). *Nigerian Journal of Paediatrics*, **6(1), 1. Burkitt's Lymphoma in Children at Ibadan: A review of 133 cases.** A review of 133 children with Burkitt's lymphoma admitted to the University College Hospital, Ibadan, during a ten-year period has revealed a preponderance of males over females and a peak age incidence of seven years. The main sites affected initially by the tumour in order of frequency were the abdomen, the face and the spinal column. The spleen, the lungs and the peripheral lymph nodes were found to be more frequently involved than has been reported in the literature. It is postulated that an interaction between malarial and EB virus infections and malnutrition are important factors in the aetiology of the tumour.

While working in Uganda, Burkitt (1958) described a common childhood lymphoma which today bears his name. Since then, there have been reports from various parts of Africa on the clinical, pathological and radiological features of the lymphoma (O' Conor and Davies, 1960; Wright, 1963; Edington and Maclean, 1964; Pulvertaft 1964; Cockshott, 1965; Osunkoya, 1968; Osunkoya and Ajayi, 1972/73). Outside Africa, a few cases of the tumour have also been reported (Booth *et al.*, 1964; O'Conor, Rappaport and Smith, 1965; Dorfman, 1965; Gravell *et al.*, 1976; Gotlieb-Stematsky, *et al.*, 1976).

Previous reviews of childhood malignancies at the University College Hospital (UCH), Ibadan, Nigeria, have established that Burkitt's lymphoma is the commonest tumour of childhood (Sinnette, 1967; Williams, 1975). The present communication is a review of cases of the lymphoma admitted to the UCH between 1964 and 1973. It examines the clinical pattern and prognosis of the disease and also details some aspects of the tumour not previously emphasized.

Materials and Methods

The case notes of children admitted to the department of Paediatrics with the clinical diagnosis of Burkitt's lymphoma, during the ten-year period (January, 1964 to December, 1973) were examined. The present study only reviews those cases in which the diagnosis was confirmed cytologically, histologically and/or at necropsy. The review does not include few cases whose case notes could not be retrieved neither does it include a few others who, by their dramatic reponse to cyclophosphamide therapy, were most likely cases of Burkitt's lymphoma but

were not so proven by any of the above criteria. An analysis of the necropsy findings of cases which came to autopsy was also undertaken.

Results

According to the Ibadan Cancer Registry, 241 childhood cases of Burkitt's lymphoma, were diagnosed at the UCH during the period under review. Of this number, 158 were males and 83 were females, a ratio of 1.9:1. Their ages ranged between two years and thirteen years, and the peak age incidence was seven years. One hundred and thirty three of the 241 cases fulfilled the above criteria.

Age and Sex distribution

There were 83 males and 50 females giving a male/female ratio of 1.7:1, thus confirming the male preponderance over female. Figure 1 shows the age distribution in the series. The youngest patient was three years old, while the oldest was thirteen. The peak age was seven years, and eighty-five (64 per cent) of the patients were between the age of five and nine years.

Social background

The occupations of the fathers were recorded in 121 cases. Fifty-one (42 per cent) of these fathers were subsistence farmers with no formal education. Twenty-one other fathers (20 per cent) were traders, while 45 others (37 per cent) were self-employed drivers, tailors, carpenters, barbers or casual labourers. Only one father, (an assistant superintendent in the police force) had a relatively high income. It seems obvious therefore, that a majority of these fathers were in the low income group of the society.

Duration of symptoms

The duration of symptoms before presentation (Table I) was given by 125 patients. Of these, 85 (68 per cent) presented within two months, while 118 (94 per cent) presented within four months from the onset of symptoms.

TABLE I

Duration of Symptoms in 133 Cases of Burkitt's Lymphoma

Duration (months)	*No. of cases*	*No. of Deaths*	*Per cent Mortality*
0 – 1	44	31	70
1 – 2	41	36	88
2 – 3	22	16	73
3 – 4	11	9	82
4 – 5	5	3	60
5 – 6	1	0	0
6 – 7	2	1	50
Unstated	7	7	100
Total	133	103	77

Tumour Manifestation

Table II summarizes the different sites affected by the tumour, which manifested initially in three major parts of the body, namely: the face, the abdomen, and the spinal column. A number of children however, had mixed sites of presentation.

TABLE II

Sites affected in 133 Cases of Burkitt's Lymphoma at Initial Presentation

Site	*No. of cases*	*No. of deaths*	*Per cent mortality*
Abdomen only	71	57	80
Abdomen and face	12	10	83
Abdomen and lungs	3	3	100
Abdomen, face and CNS	2	2	100
Abdomen and subcutaneous tissue of the abdomen	1	1	100
Abdomen, face and subcutaneous tissue of the abdomen	1	1	100
Abdomen and spinal column	1	1	100
Face only	22	16	73
Face and CNS	5	3	60
Face and cervical glands	2	2	100
Face and spinal column	2	1	50
Face and glands in the groins	1	1	100
Face and thyroid	1	1	100
Spinal column only	7	2	29
Knee alone	2	2	100
Total	133	103	77

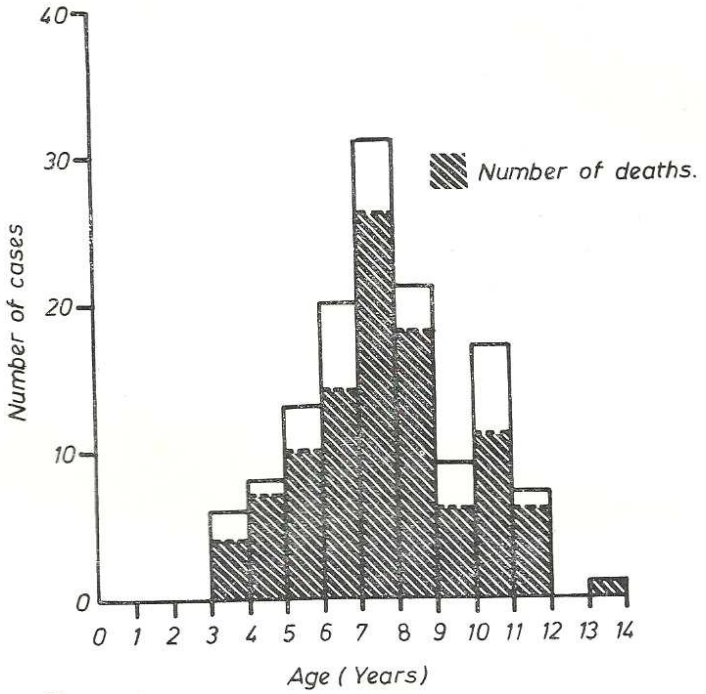

Fig. 1. Age distribution in 133 cases of Burkitt's lymphoma

Facial Presentation

Twenty–two (17 per cent) of the 133 cases (17 males and 5 females) presented with facial tumours only. They were aged between three and ten years with a peak at *five* years. The duration of symptoms varied between four days and five months; seventeen (77 per cent) of the 22 cases presented within three months. Associated signs in some of the patients included ulceration and bleeding of the affected cheek and gum, ophthalmoplegia, blindness and deafness. Looseness of teeth in the affected jaw was usually demonstrated by gently prodding with a spatula. In many advanced cases, there was disorganization of the normal dental alignment (dental anarchy). In five patients the tumour later involved the central nervous system (CNS), while one case developed an abdominal tumour. Significant lymphadenopathy involving the cervical (4 cases) axillary (5 cases), and inguinal (3 cases) nodes occurred in some patients.

In 12 of the patients, the spleen was enlarged, while there was hepatomegaly in nine. Most of the patients were malnourished.

Abdominal Presentation

Seventy-one (53 per cent) out of the 133 cases presented initially with abdominal symptoms. They consisted of 39 males and 32 females and the age ranged between three and thirteen years, with a peak at seven years. Fifty-nine (83 per cent) of the 71 cases presented within three months (range, 2 weeks – 6 months) of onset of symptoms.

The most common presenting symptom, occurring in 65 (92 per cent) of the patients, was progressive abdominal swelling. In the remaining six children, there was no history of abdominal swelling. In 35 cases, the abdominal swelling was accompanied by continuous or colicky abdominal pains. Other prominent complaints in these patients were loss of weight, fever, anorexia and vomiting.

On examination, hard and craggy abdominal masses were found in 60 of the 71 cases. These were usually single but in a few cases, they were multiple. There was hepatomegaly in 20 and splenomegaly in 12 cases. Ascites was present in 32 cases. In addition to the abdominal signs, two cases had generalised lymphadenopathy and significant localised lymphadenopathy was present in 5 cases. All except one of the 71 patients were wasted.

Among these 71 patients, eight were initially diagnosed as cases of abdominal tuberculosis. The correct diagnosis was subsequently made during life in four of these, but the remaining four cases received anti-tuberculous therapy until death and the diagnosis of lymphoma was made finally at necropsy. Sixteen of the 71 cases subsequently developed tumours at one or more other sites (5, facial; 2, meningeal; 2, cutaneous deposits; and 5, multiple sites).

Figure 2 compares the number of patients with initial abdominal and facial tumours. It will be observed that between 1964 and 1968 there were as many cases with facial presentation as abdominal ones, but there were more abdominal cases than facial ones between 1969 and 1973.

Spinal Presentation

Seven cases (5 males and 2 females), aged between 5 and 10 years (peak age, 6 years), presented initially with involvement of the spinal column. All of them presented within 2 months of onset. Inability to stand, usually of sudden onset, was the presenting symptom in all cases. There was incontinence of urine and faeces in two cases, and incontinence of urine alone in another case. There were five cases of flaccid and two of spastic paraplegia. Two of these cases also had significant lymphadenopathy. In all the cases, the tumour later involved other sites: jaw (4 cases), abdomen (2 cases), and retro-orbital tissues (1 case).

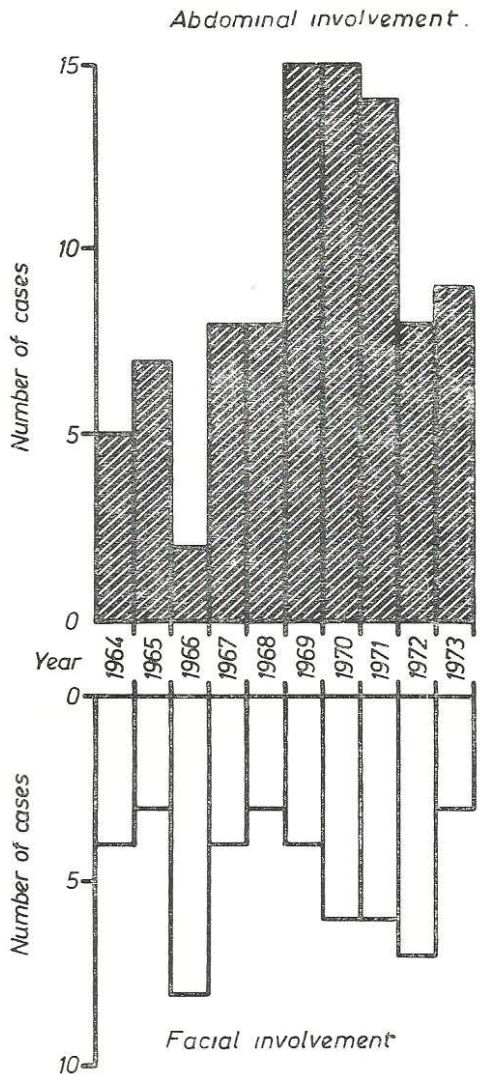

Fig. 2. Number of patients with initial facial and abdominal tumours. Note that between 1964 and 1968 there were as many cases with facial as abdominal ones, but there were more abdominal cases than facial ones between 1969 and 1973.

Mixed Presentations

Thirty-three patients were considered to have mixed presentation on initial evaluation. Twenty-six presented with facial tumour as well as additional tumours at other sites (abdomen, CNS, spine, thyroid, and abdominal subcutaneous

tissue). Thus, in 48 cases (22 with facial presentation alone plus 26 with mixed presentation), the face was involved. There were 20 patients with tumours in the abdominal cavity and elsewhere (face, skin, CNS, lungs), thus resulting in a total of 91 cases with abdominal tumours either as sole presentation or combined with tumours at other sites. Forty-nine (54 per cent) of these 91 cases had ascites. Ten patients had spinal tumours in combination with tumour elsewhere; thus there was a total of seventeen cases with spinal tumour.

Three children presented with pleural effusion diagnosed initially as tuberculous effusion. Cytological examination of the fluid which was haemorrhagic in one case and straw-coloured in the remaining two cases, yielded Burkitt lymphoma cells.

Laboratory Investigations

Diagnostic Procedures: These included cytology (most often by phase contrast technique) of the peritoneal fluid, biopsies and histological examination of the solid tumour, and cytology of tumour aspirates. Other diagnostic procedures were bone marrow and liver biopsies, lymph node biopsy, and cytological examination of CSF. The histology in each case revealed the characteristic lymphoma cells (Fig. 3).

Radiological Findings

Jaw: X-rays of the jaws were done in 37 cases and in 19 of these, including three with small jaw tumours, the films were normal. In the remaining 18 cases, including five with no visible jaw tumour, there was loss of lamina dura. In addition to the involvement of the lamina there were osteolytic lesions in various parts of the mandible, maxilla, and the zygoma (Fig.4). Three out of eight patients with initial abdominal tumour had X-rays of the jaws which showed loss of lamina dura; these subsequently developed facial tumours.

Chest: Thirty-six patients had chest x-rays which were normal in 18. In eight cases, there was consolidation, collapse or bronchopneumonia. Four films showed pleural effusion and five others revealed paravertebral swelling.

There was one case of cardiomegaly, which at necropsy was found to be due to tumour deposits in the myocardium and pericardium.

Spinal column: Spinal radiograph was undertaken in eight children and this was normal in seven. The abnormal case revealed patchy destruction of D9.

Other radiological procedures: Intravenous pyelogram was performed in 20 cases with abdominal presentation, and in six with facial presentation. The procedure was normal in nine patients and in the remaining 17 cases, there was either non-excretion of contrast material or distortion of the calyces (Fig. 5). While these abnormalities occurred mainly in patients presenting with abdominal tumours, it is noteworthy that there was non-excretion of contrast material in two cases presenting with facial tumour. Myelography was carried out in three patients who presented with flaccid paraplegia. There were partial blocks at D3 and D9 in one case, and complete blocks at C5 and T2 respectively in the remaining two cases (Fig. 6). The procedure was normal in the remaining patient. Abdominal aortography undertaken in two patients with abdominal tumours, revealed abnormal vascularization around the tumour.

Haematology: The average PCV (haematocrit) was 31 per cent (range, 9-47 per cent). Forty (35 per cent) of 115 children had values below 30 per cent. In five patients with proven bone marrow involvement, the average PCV was 16 per cent (range, 9-22 per cent). The average total white cell count in these five patients was 37,550/c.mm (range, 7,400–59,700/c.mm). The differential count revealed the presence of blast cells in the peripheral blood of three patients who also had thrombocytopaenia. Haemoglobin electrophoresis was determined in 69 patients and this revealed 48 cases (69.6 per cent) of A; 13 (18.8 per cent) AS; 7 (10 per cent) AC, and 1 (1.5 per cent) SC. This distribution is not significantly different from that of the general population

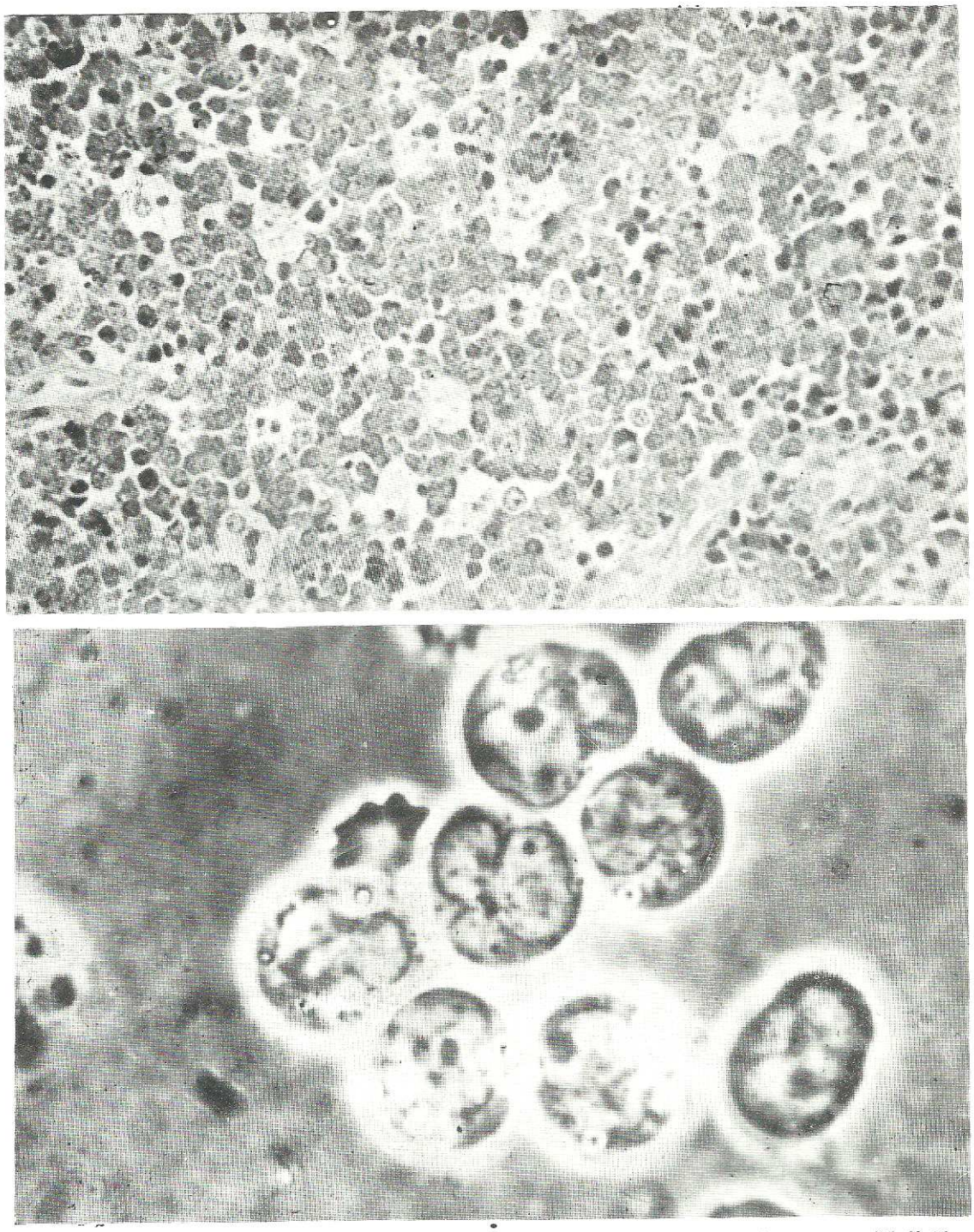

Fig. 3. Photomicrograph of a histological section of the lymphoma showing the typical starry-sky appearance (H & E)

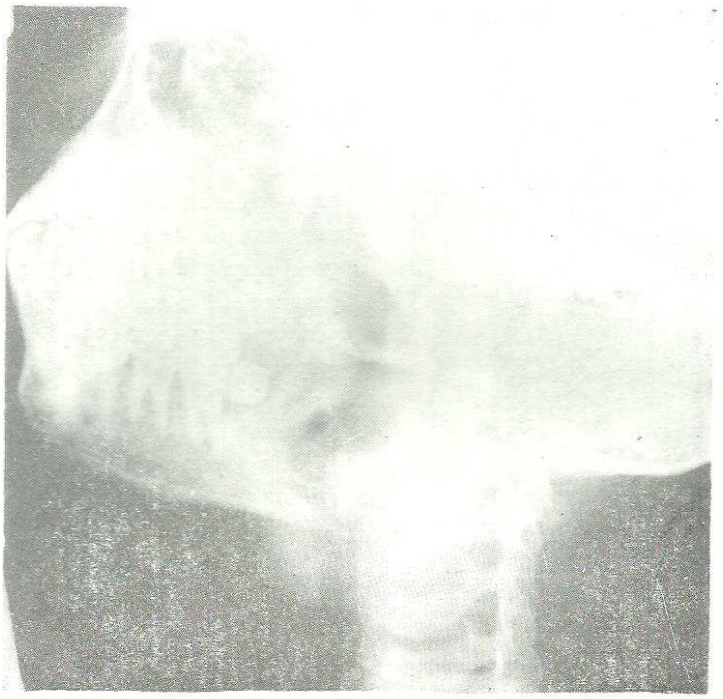

Fig. 4. Radiograph of the jaw bones in a patient with facial tumour. There is loss of lamina dura in the lower premolar and molar teeth.

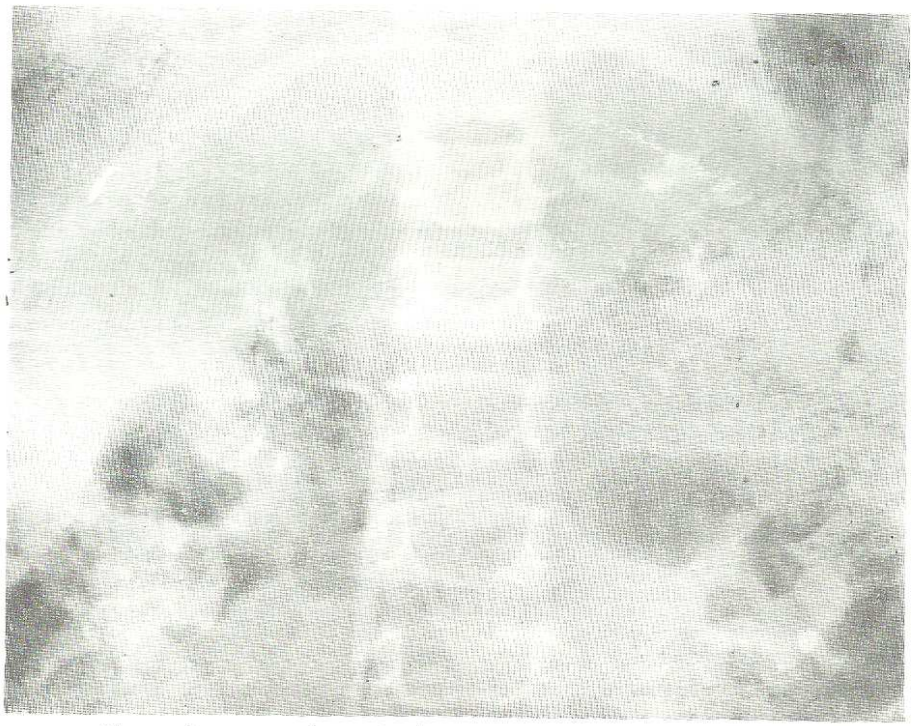

Fig. 5. Intravenous pyelogram showing poor excretion and distortion of the calyces.

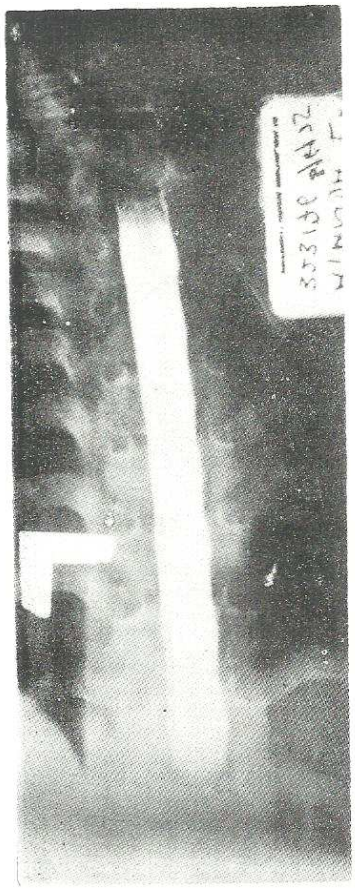

Fig. 6. Myelogram of a patient with spinal tumour. Note the block at T2.

(Walters and Lehmann, 1956; Esan, 1978 personal communication).

Management and Response

Specific treatment: The standard treatment consisted of cyclophosphamide (Endoxan) administered intravenously (10-15 mg/kg body weight/day) for 7-10 days. In 4 cases, the drug was given as an infusion in a single dose of 40 mg/kg body weight. Other drugs tried at various times as alternatives to cyclophosphamide included nitrogen mustard, cytosine arabinoside, methotrexate (intravenous, oral, and intrathecal) and colcemid. Nephrectomy, carried out both as a diagnostic and therapeutic procedure, was performed on a child with a renal tumour; excision biopsy was also performed on another child with an orbital tumour.

Initial response to treatment

Abdominal tumours: Response to chemotherapy was evaluated in 52 patients with abdominal tumours. Of these, 25 (48 per cent) had very good response as judged by the complete disapperance of the tumour within 7-14 days (average, 9 days). Eighteen (35 per cent) others had no response and in the remaining nine cases, there was initially a partial reduction in the size of the tumour, but this response was soon followed by a relapse even though the patients were still on treatment.

Facial tumour: Twelve (55 per cent) out of 22 patients had a good response, the tumour shrinking within 6-7 days (average 6.5 days). Six others had moderate reduction in the size of the tumour, while there was no appreciable response in four. Two others had initial good response but the tumour became static in one case and in the second case it even grew larger.

Spinal tumour: There was a very good response in four of the seven children presenting with paraplegia and inability to stand. They were able to walk again within two weeks of therapy with intravenous cyclophosphamide and intrathecal methotrexate. In two others with paraplegia, faecal and urinary incontinences, initial improvement consisted of restoration of continence only.

Therapy with cytotoxic drugs, especially cyclophosphamide, produced reduction in the total white cell count which usually occurred between 7 and 14 days of therapy and sometimes was quite profound. The total white cell count fell below 2000/cmm in 29 cases and there were two patients whose counts fell to 400/cmm, and two others with counts of 200 and 100/cmm respectively. Other side-effects which were frequently encountered particularly with cyclophosphamide included partial or total alopecia, hyperpigmentation of the skin and oral mucous membranes, and dark bands across the finger and toe nails (Fig.7).

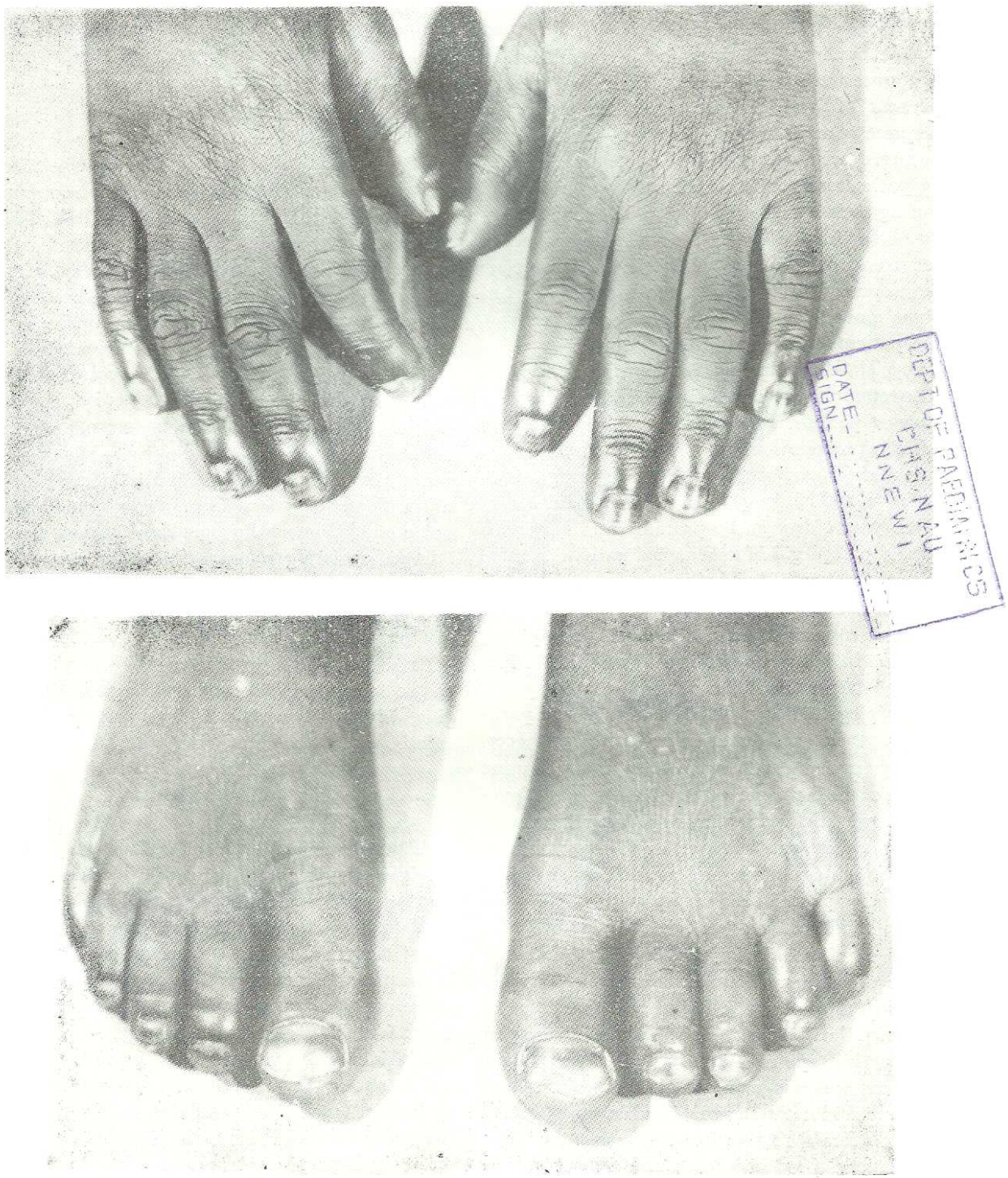

Fig. 7. Cyclophosphamide-induced dark bands across the finger and toe nails.

Course and Outcome

One hundred and three (77 per cent) of the 133 cases were known to have died, and 72 (70 per cent) of these deaths occurred within 3 months of presentation. Although most of these deaths occurred within a few weeks of presentation, 23 patients responded satisfactorily to treatment during their initial admission and were discharged home. All these were readmitted with either recurrence of the tumour at the initial site or development of tumours at other sites within eight months of discharge; 21 (91 per cent of the patients were readmitted within six months. They all died during the second admission. The remaining 30 survivors were followed up for varying periods. Twenty-three of these survivors were lost to follow–up after six months, but seven survived for over six months before being lost to follow–up. The longest known survivor was a three–year old boy who presented initially with flaccid paraplegia of four days duration. He was still alive four and a half years later.

Fourteen cases who initially had no neurological involvement later developed paraplegia (flaccid in 10, and spastic in four others) while on treatment. One other child developed spastic quadriplegia. All ten children with flaccid paraplegia developed incontinence of urine and faeces. In eight patients, there was a lower motor neurone lesion of the facial nerve. One patient each developed 3rd, 4th, and 6th nerve palsies respectively and another one became deaf. Six children became blind and one had a saddle anaesthesia. Burkitt lymphoma cells were present in the CSF in ten children. Non-neurological manifestations which developed during the course of the disease while the patients were on treatment included seven cases of pleural effusion, and five cases of skin nodules (Fig. 8). Eight children developed obstructive type of jaundice. One of these eight children was a 7-year old girl with abdominal tumour and total serum bilirubin of 15.2 mg/100 ml (direct, 10.1 mg/100 ml) who, a day after admission lapsed into coma and never regained consciousness until she died nine days later. Some degree of renal dysfunction (serum urea levels ranging between 50 and 117 mg/100 ml) occurred in 13 patients.

Necropsy Findings

Fifty-seven (55 per cent) of the 103 who died underwent post-mortem examination. The organs and sites involved are listed in Table III. The most commonly involved organs were the kidneys, liver, lymph nodes, gastro-intestinal tract, adrenals, spleen, pancreas, heart and ovaries. It is noteworthy that the lung parenchyma was involved in six cases and the brain tissue in six other cases. The lymph nodes involved were mainly those in the abdominal cavity, but in eight cases, the mediastinal nodes were involved and in three cases each, the cervical and axillary nodes were affected. The cut surface of the involved node usually had a fleshy white appearance. Sometimes, these nodes were matted and necrotic. Ulceration of the gastro-intestinal tract, especially the stomach was present in eight cases. The gastric ulcer perforated in one case. The rectum was involved by the tumour in one case. Haemopericardium was documented in one patient. In two cases, there was terminal pyogenic meningitis, while one patient had pulmonary tuberculosis.

Discussion

Although the incidence of Burkitt's lymphoma in Nigeria is unknown, there can be no doubt that it is the commonest malignant tumour in childhood (Edington and Maclean, 1964; Sinnette, 1967; Williams, 1975). The peak age incidence in the present series as well as in those reported by others in Ibadan was seven years (Sinnette, 1967; Osunkoya and Ajayi, 1972/73). The peak age incidence of five years among patients with facial tumour was however similar to thatreported by Burkitt (1958). This tendency for the tumour to involve the facial tissues in younger children is an intriguing aspect of the disease which requires further studies. Similarly, response to treatment

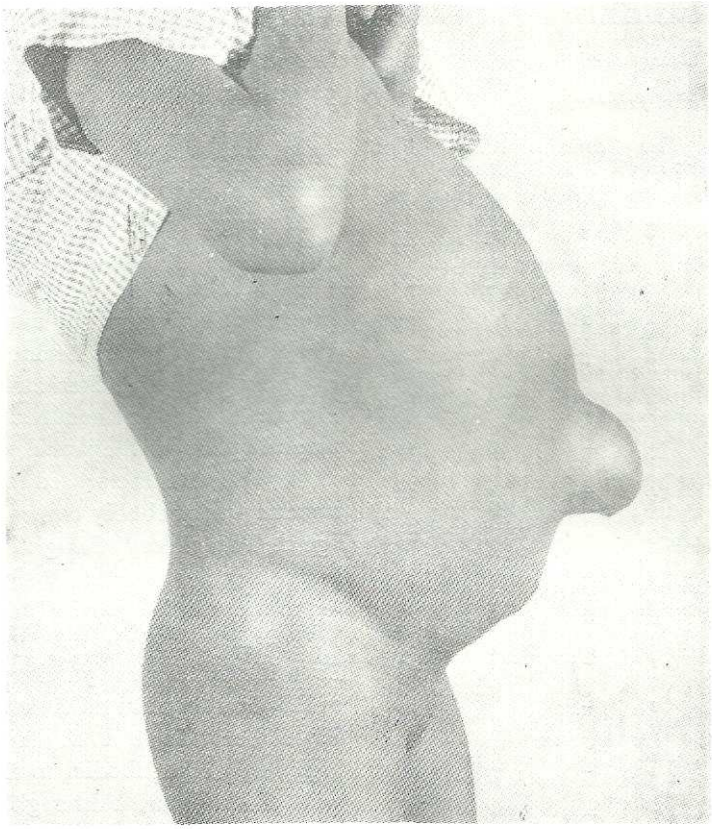

Fig. 8. Tumour deposit in subcutaneous tissue below the large umbilicus.

was more rapid among those with facial tumour; the average number of days for appreciable regression of facial tumours was five days compared to an average of nine days among those with abdominal tumour.

Burkitt (1962), Ngu (1967) and Wright (1967) reported jaw tumours as being more common than abdominal ones. Our experience, however, shows that in the early years of the present review (1964-1967) facial tumours were as common as abdominal tumours, while during the period 1968-1973, abdominal tumours were more common (Fig. 2). This finding accords with those of Sinnette (1967) and Cohen *et al.* (1969). The facial manifestation of the disease is striking and would thus tend to make patients seek early medical attention. This may also explain the earlier reported higher incidence of the facial manifestation than others. Indeed, Burkitt (1962) has also considered this possibility.

Several authors (Burkitt, 1962; Cockshott, 1965; Janota, 1966; Ngu, 1967; Sinnette, 1967) have reported that the tumour rarely involves the spleen, lung parenchyma, brain tissues and the peripheral lymph nodes. It is clear from the present review that these sites are not immune from the tumour. Involvement of these organs is however, relatively uncommon but it is not rare. Recently, Aderele, Seriki and Osunkoya (1975) reported 4 cases of pleural effusion due to the tumour. Necropsy findings in the present review have also revealed involvement of the lung parenchyma (six cases), spleen (22 cases), peripheral lymph nodes (15 cases) and brain tissue (six cases).

TABLE III

Necropsy Findings in 57 Cases of Burkitt's Lymphoma

Site	Clinical Presentation: Abdomen (28 cases)	Face (10 cases)	Spinal Column (1 case)	Mixed (18 cases)	Total
Kidneys	23	8	1	13	45
Liver	17	5	1	13	36
G. I. tract	13	2	1	14	30
Lymph nodes	18	5	–	7	30
Adrenals	11	4	1	8	24
Peritoneum	14	–	–	8	22
Spleen	13	4	–	5	22
Pancreas	10	3	–	8	21
Heart	10	2	–	6	18
Ovaries	7	2	–	5	14
Pleura	9	1	–	3	13
Orbital tissues	2	1	–	7	10
Retroperitoneum	2	1	–	7	10
Thyroid	2	1	–	6	9
Jaw	2	4	–	2	8
Diaphragm	3	–	–	4	7
Lungs	2	1	–	3	6
Brain	1	4	–	1	6
Bladder	4	–	1	1	6
Pleura	4	–	–	1	5
Pericardium	3	–	–	2	5
Bone marrow	4	1	–	–	5
Other sites:-	Epidural space, Porta hepatis, Vagina, Uterus, Mesentery, Testes, Portal vein, Sphenoid bone, Femur, Ribs, Meninges, Spinal cord nerves, Chorda equina.				

In 1970, Ziegler *et al.*, proposed a clinical staging of Burkitt's tumour. The widespread nature of the tumours even at first presentation however makes any correlation between the proposed clinical staging and prognosis unsatifactory. As shown in this reveiw, some of those who initially presented with facial lesions were later proven at necropsy to have widespread disease (Table III). In the light of our present experience it is suggested that the clinical staging of the tumour should be reviewed.

Although Burkitt's lymphoma has been reported mainly from Africa and New Guinea (Ten Seldam *et al.*, 1965; Burkitt, 1967), cases have also been described from other parts of the world (Burkitt, 1967; Levine *et al.*, 1972; Cohen *et al.*, 1969; Gotlieb-Stematsky *et al.*, 1976). The tumour is thus not confined to the warm and tropical parts of the world where the existence of these climatic factors led to the theory that the tumour was probably caused by a vector-borne agent. This theory though invalidated by some inconsistencies (Burkitt, 1969), has nevertheless led to the search for a viral aetiology. This search bore fruit in 1964 when Epstein, Achong and Barr identified virus particles (the Epstein-Barr or EB virus) in cultured Burkitt's lymphoma cells. Since then, Henle *et al.* (1976) have reported high levels of antibodies to the virus in patients with the tumour. Although a causal relationship has not been irrefutably proven, evidence so far suggests that the virus is involved in the pathogenesis of Burkitt's lymphoma. Another factor which has been incriminated in the aetiology of the tumour is severe malaria infection (Kafuko *et al.*, 1961; Burkitt 1969; Kafuko and Burkitt, 1970). Morrow *et al.* (1976) have postulated that severe malaria infection is important not only in the development of the tumour, but also in precipitating its onset.

The current concept therefore is that both EB virus and severe malaria infection are involved in the pathogenesis of the lymphoma. We believe that this is probably not the whole answer to the problem. While severe malaria infection may be incriminated in patients living in malarial endemic parts of Africa, the same cannot be said for those patients in the non-malarious regions of the world; nor does it provide the whole answer even within Nigeria where the incidence of the disease varies from place to place within the same

malarious belt. If the tumour were mainly due to the interaction of malaria infection and the EB virus, one would expect similar prevalence of the tumour in areas of Nigeria with identical climatic conditions, but our experience as well as that of Osunkoya and Ajayi (1972/73) is that the incidence of the tumour varies widely within the same geographical and climatic areas of the country. It seems pertinent therefore that other contributory factors should be examined. It has been observed from this review that 99 per cent of the children were of low socio-economic background. It is in this same class of the society that the highest incidence of undernutrition occurs. Children who suffer from all forms of malnutrition also have a higher incidence of infections than the well-nourished ones. It is therefore postulated that frequent and almost continuous stimulation of the immune systems of these malnourished children by malaria and other infections, leave the systems too weak qualitatively, to combat the EB virus. As a consequence, the lymphoproliferative activities of the virus cannot be effectively checked. In order to establish this postulated interaction of virus and malaria infections and nutrition, epidemiological, immunological and nutritional studies are required.

It is suggested that in order to reduce the incidence of this common childhood tumour there should be improvement in the standard of living of the population as well as eradication of malaria infection. It is recognised that these are long-term objectives. In the short term however, widespread use of malaria prophylaxis may help in reducing the incidence of the tumour as it has apparently done in parts of Uganda (Morrow *et al.*, 1976). Another measure would be the development and widespread use of anti-EB virus vaccine as has been suggested by Epstein (1976).

Acknowledgements

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References

Aderele, W. I., Seriki, O. and Osunkoya, B. O. (1975). Pleural effusion in Burkitt's lymphoma. *Brit. J. Cancer*, **32**, 745–746.

Booth, C. C., Davies, J. N. P., Hutton, P., Fraser, R., Harris, R. J. C., Lehner, T., Chesterman, F. C. and Negroni, G. (1964). A case of African lymphoma. Demonstrated at the Postgraduate Medical School of London. *Brit. Med. J.*, **1**, 296–299.

Burkitt, D. (1958). A sarcoma involving the jaws in African children. *Brit. J. Surg.*, **46**, 218–223.

Burkitt, D. (1962). A tumour syndrome affecting children in Tropical Africa. *Postgrad. Med. J.*, **38**, 71–79

Burkitt, D. P. (1967). Burkitt's lymphoma outside the known endemic areas of Africa and New Guinea. *Int. J. Cancer*, **2**, 562–565.

Burkitt, D. P. (1969). Etiology of Burkitt's lymphoma — an alternative hypothesis to a vectured virus. *J. Natl. Cancer Inst.*, **42**, 19–28.

Cockshott, W. P. C. (1965). Radiological aspects of Burkitt's tumour. *Brit. J. Radiol.*, **38**, 172–180.

Cohen, M. H., Bennett, J. M., Berard, C. W., Ziegler, J. L., Vogel, C. L., Sheagren, J. N. and Carnone, P. P. (1969). "Burkitt's tumour" in the United States. *Cancer*, **23**, 1259–1272.

Dorfman, R. F. (1965). Childhood lymphosarcoma in St. Louis, Missouri, clinically and histologically resembling Burkitt's tumour. *Cancer*, **18**, 418–430

Edington, G. M. and Maclean, C. M. U. (1964). Incidence of the Burkitt's tumour in Ibadan, Western Nigeria. *Brit. Med. J.*, **1**, 264–266.

Epstein, M. A., Achong, B. G. and Barr, Y. M. (1964). Virus particles in cultured lymphoblasts from Burkitt's lymphoma. *Lancet*, **1**, 702–703.

Epstein, M. A. (1976). Epstein-Barr Virus - Is it time to develop a vaccine program? *J. Natl. Cancer Inst.*, **56**, 697–700.

Gotlieb-Stematsky, T., Ramot, B., Vonsover, A., Aghai. E., Kende, G., Ninio, M. and Modan, M., (1976). Antibodies to Epstein–Barr viral capsid and early antigens associated with Burkitt's lymphoma and lymphoblastic lymphosarcoma in Israel. *J. Natl. Cancer Inst.*, **56**, 721–723.

Gravell, M., Levine, P. H., McIntyre, R. F., Land, V. J. and Pagano, J. S. (1976). Epstein–Barr virus in an American patient with Burkitt's lymphoma: Detection of viral genome in tumour tissue and establishment of a tumour-derived cell line (NAB). *J. Natl. Cancer Inst.*, **56.**, 701–704.

Henle, G., Henle, W., Clifford, P., Diehl, V., Kafuko, G. W., Kirya, B. G., Klein, G., Morrow, R. H., Munube, G. M. R., Pike, M. C., Tukei, P. M. and Ziegler, J. L. (1969). Antibodies to EB virus in Burkitt's lymphoma and control groups. *J. Natl. Cancer Inst.*, **43**, 1147–1157.

Janota, I. (1966). Involvement of the Nervous System in Malignant Lymphoma in Nigeria. *Brit. J. Cancer*, **20**, 47–61.

Kafuko, G. W., Baingana, N., Knight, E. M. and Tibemanya, J. (1969). Association of Burkitt's tumour and holoendemic malaria in West Nile district, Uganda: malaria as a possible aetiologic factor. *E. Afr. Med. J.*, **46**, 414–436.

Kafuko, G. W. and Burkitt, D. P. (1970). Burkitt's lymphoma and malaria. *Int. J. Cancer*, **6**, 1–9.

Levine, P. H., O'Conor, G. T. and Berard, C. W. (1972). Antibodies to Epstein-Barr virus (EBV) in American patients with Burkitt's lymphoma. *Cancer*, **30**, 610–615.

Morrow, R. H., Kisoule, A., Pike, M. C. and Smith, P. G. (1976). Burkitt's lymphoma in the Mengo districts of Uganda: epidemiologic features and their relationship to malaria. *J. Natl. Cancer Inst.*, **56**, 479–483.

Ngu, V. A. (1967). The African lymphoma or the Burkitt tumour. *W. Afr. Med. J.* **17**, 189–197.

O'Conor, G. T. and Davies, J. N. P. (1960). Malignant tumours in African Children with special reference to malignant lymphoma. *J. Pediat.*, **56**, 526–535.

O'Conor, G. T., Rappaport, H. and Smith, E. B. (1965). Childhood lymphoma resembling "Burkitt tumour" in the United States. *Cancer*, **18**, 411–417.

Osunkoya, B. O. (1968). The histopathology, cytology and immunology of Burkitt's lymphoma. *W. Afr. Med. J.*, **17**, 268-270

Osunkoya, B. O. and Ajayi, O. O. (1972/73). Burkitt's lymphoma. A clinico-pathological review of Ibadan cases. *Pediatrician*, **1**, 261–271.

Pulvertaft, R. J. V. (1964). Cytology of Burkitt's tumour (African lymphoma). *Lancet*, **1**, 238–240.

Sinnette, C. H. (1967). Childhood malignancies. Report from a West African Teaching Hospital with special emphasis on Burkitt's tumour. *Clin. Pediat.*, **6**, 721–727.

Ten Seldam, R. E. J., Cooke, R. and Atkinson, L. (1966). Childhood lymphoma in the territories of Papua and New Guinea. *Cancer*, **19**, 437–446.

Walters, J. H. and Lehmann, H. (1956). Distribution of S and C haemoglobin variants in two Nigerian communities. *Trans. R. Soc. Trop. Med. Hyg.*, **50**, 204–208.

Williams, A. O. (1975). Tumours of Childhood in Ibadan, Nigeria. *Cancer*, **36**, 370–378.

Wright, D. H. (1963). Cytology and Histochemistry of the Burkitt's lymphoma. *Brit. J. Cancer*, **17**, 50-55.

Wright, D. H. (1967). Burkitt's tumour and Childhood lymphosarcoma. *Clin. Pediat.*, **6**, 116–123.

Ziegler, J. L., Morrow Jr., R. H., Fass, L., Kyalwazi, S. K. and Carbone, P. P. (1970). Treatment of Burkitt's tumour with cyclophosphamide. *Cancer*, **26**, 474–484.