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## HODGKIN'S DISEASE IN ZAMBIA

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### SUMMARY

A five-year (1970-74) retrospective study has been carried out in the Department of Pathology to determine the histological and epidemiological pattern of Hodgkin's disease in Zambia.

Hodgkin's disease constituted 18.6% (38 cases) of lymphomas, 44% of the cases being seen in the first two decades of life. The male: female ratio was 2.8:1. Most of the cases were either in Stage II or Stage III. Mixed cellularity and lymphocytic depletion represented the commonest histological types.

Aetiological and epidemiological factors are discussed.

### INTRODUCTION

Hodgkin's disease occurs throughout the world with wide variation in incidence rates (1, 2). The pattern of the disease has not previously been studied in Zambia. We have undertaken this study to evaluate the incidence of Hodgkin's disease and to compare our results with those reported from various parts of the world.

### MATERIALS AND METHODS

The University Teaching Hospital, Lusaka, provides the diagnostic histological services to the Central, Eastern, Western and Southern Provinces of Zambia, covering approximately 53% (2.5 million) of the Zambian population. The patients in this study were representative of an unselected African population of all ages in the above provinces. The 1969 Zambia population census figures were used for standardization rates (3).

All tumours classified as Hodgkin's disease for the 5-year period 1970 to 1974 were reviewed. Sections were examined by both of us and classified according to the criteria of the Rye modification of the Lukes-Butler classification (4). Diagnosis of nodular sclerosis was based on the presence of lacunar variant of the Sternberg-Reed cell and complete or incomplete bands of collagen formation with or without production of distinct nodules.

### RESULTS

In our review of all malignant tumours we found 218 cases of malignant lymphoma of which 46 were classified as Hodgkin's disease. One was excluded from the study because of inadequate biopsy material for a definite diagnosis. Of the remaining 45 cases, 7 cases were reclassified as not Hodgkin's (Table 1). The remaining 38 cases were confirmed as Hodgkins disease. Hodgkin's disease (19%) formed the smallest group of all malignant lymphomas (Table 2). Our finding is similar to that of Wright in Uganda (5).

Table 1

*Misdiagnosis of Hodgkin's disease*

<i>Revised diagnosis</i>	<i>No. of cases</i>
Reactive lymphadenopathy .. .. .	1
Sinus histiocytosis (SHML) .. .. .	1
Stem-cell lymphoma .. .. .	1
Histiocytic lymphoma .. .. .	3
Anaplastic tumour .. .. .	1
Total .. .. .	7.45 (15.5%)

Table 2

*Incidence of malignant lymphomas Zambia 1970-1974*

<i>Histological type</i>	<i>No. of cases</i>	<i>%</i>
Lymphocytic well differentiated (WD)	27	13
Lymphocytic, poorly differentiated (PD)	39	19
Histiocytic .. .. .	36	18
Stem-cell .. .. .	14	7
Burkitt .. .. .	44	21
Hodgkin's disease .. .. .	38	19
Lymphoma (unclassified) .. .. .	6	3
Total .. .. .	204	100

*Age and sex distribution*

The age and sex distribution of 38 reclassified cases of Hodgkin's disease is shown in Table 3. The majority of the patients (53%) with Hodgkin's disease were under 30 years of age. The youngest patient was 6 years and the oldest 67 years.

The age distribution in our study revealed a significant difference from similar studies in other countries. The majority of our cases were in a younger age group than reported from Europe and U.S.A. (Table 3).

The incidence for Zambian age-standardized rates were compared with similar studies in other countries. These are shown in Tables 4 and 5. The rate in Zambia was low compared to those in Nigeria, United

Table 3

*Age and sex pattern of Hodgkin's disease*

<i>Age (years)</i>	<i>Male</i>	<i>Female</i>	<i>M:F</i>	<i>Total</i>
0-9	4	1	4:1	5
10-19	8	1	8:1	9
20-29	5	1	5:1	6
30-39	2	3	0.6:1	5
40-49	2	3	0.6:1	5
50-59	3	0	3:0	3
60-69	4	0	4:0	4
Unknown	0	1	0:1	1
Total	28	10	2.8:1	38

Kingdom, and U.S.A. (whites). Our lower rate may be partly due to underreporting but more probably due to real geographical variation. The age-specific incidence of Zambian and English cases are compared graphically in Fig. 1. These figures confirm the low incidence rates in Zambia.

Table 4  
Age-standardized rates: Male

Country	Europe	World	Africa
UK: Birmingham (2)	2.9	2.7	2.8
USA: California, white (2)	3.1	2.6	2.3
USA: California, negro (2)	1.0	1.0	0.9
South Africa: Natal, Africa (2)	3.7	3.0	2.5
Nigeria: Ibadan (2)	3.7	3.2	2.5
Uganda: Wright 1973 (5)	0.5	0.5	0.5
Zambia	0.7	0.6	0.6

Table 5  
Age-standardized rates: Female

Country	Europe	World	Africa
Birmingham (3)	1.8	1.5	1.5
USA: California, white (2)	2.5	2.2	2.1
USA: California, Negro (2)	0.4	0.3	0.1
South African: Natal, Africa (2)	0.5	0.4	0.6
Nigeria: Ibadan (2)	3.0	2.4	1.6
Uganda: Wright 1973 (5)	0.2	0.2	0.2
Zambia	0.2	0.2	0.2

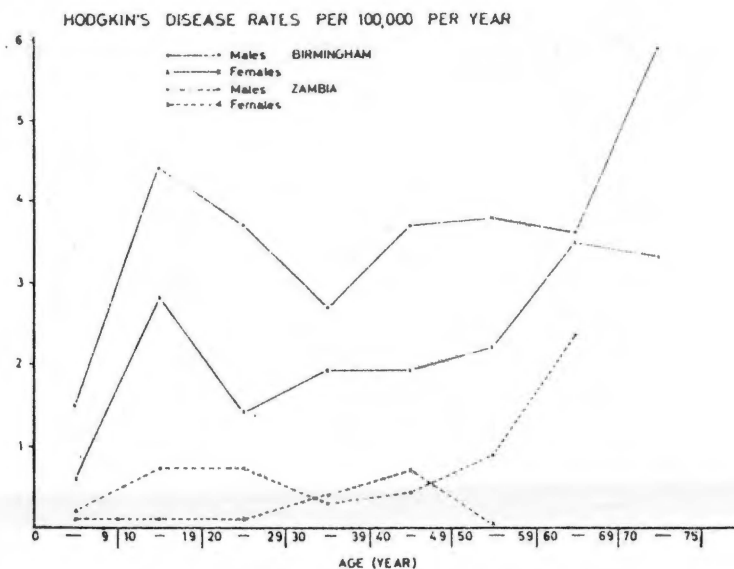


Figure 1 COMPARISON OF AGE SPECIFIC INCIDENCE RATES OF ZAMBIAN AND ENGLISH PATIENTS

Fig. 1

The sex incidence showed a male preponderance with a male: female ratio of 2.8:1. However, male preponderance was more marked in the first three decades (male: female ratio of 5.6:1). The male incidence in Zambia was nearly one-fifth that of Birmingham. Similarly, Zambian female rates remained very low in all age groups. A bimodal curve was noted in males (Fig. 1) whereas a single peak (40-49 years) was observed in females.

### *Clinical presentation*

Cervical lymphadenopathy was the most frequent presenting feature in our cases. Enlargement of cervical nodes either alone or combined with enlargement of another group of lymph nodes or supraclavicular lymphadenopathy comprised 69% of anatomical regions involved (Table 6). Clinical information was insufficient for accurate staging. Extranodal Hodgkin's disease was seen in two cases only, indicating very low incidence. The preponderance of superficial cervical lymphadenopathy as the presenting feature is almost certainly due partly to the accessibility and ease of biopsy of the site. Other factors such as infectious agents affecting portals of entry and varying lymph-node susceptibility have been suggested (6) to explain the predilection for cervical nodes.

### *Incidence of different histological types of Hodgkin's disease*

- (a) *Sex* The distribution of the various histological types is shown in Table 7. Mixed cellularity (MC) was the commonest histological type (53%) followed by lymphocytic depletion (LD) (21%) and lymphocytic predominance (LP) (16%). Nodular sclerosis (10%) was the least common type in Zambia. In all histological types male predominance (2.8:1) was noted.
- (b) The distribution of histological types of Hodgkin's disease in several countries is compared to that in our study in Table 8. Our findings as well as those of others from Africa and elsewhere suggest that the pattern of disease in developing countries differs from that described in developed countries.
- (c) *Children* The distribution of the histological types of Hodgkin's disease in Zambian, East African, and English children is compared in Table 9. There were 13 cases (34% of the total) in Zambian children (0-15 years) with a male: female ratio of 5.5:1. Mixed cellularity was the commonest histological type (62%) while LP and LD showed equal distribution (15%). However, LD was less frequent than observed in East Africa (7). The high incidence of nodular sclerosis (NS) reported from U.S.A. (8) was not seen in East and Central African children, even though Hodgkin's disease is more common in African than European and Japanese children (2).

**Table 6**  
*Main presenting sites of Hodgkin's disease in Zambia*

Site	No. of cases	%
Lymph nodes:		
cervical .. .. .	13	34
axillary .. .. .	2	5
inguinal .. .. .	5	13
multiple .. .. .	6	16
generalized .. .. .	7	19
retroperitoneal .. .. .	1	
mesenteric .. .. .	1	
Colon .. .. .	1	
Abdominal mass .. .. .	1	
Extradural space (spinal) .. .. .	1	13
Total .. .. .	38	100

**Table 7**  
*Histological classification and sex of patients*

Histological type	Male	Female	Male: Female ratio	Total	%
Lymphocytic predominance	4	2	2:1	6	16
Mixed cellularity	15	5	3:1	20	53
Nodular sclerosis	3	1	3:1	4	10
Lymphocytic depletion	6	2	3:1	8	21
Total .. .. .	28(74%)	10(26%)	2:8:1	38	100

**Table 8**  
*Comparison of histological types in various series*

Country	Percentage of histological types				No. of patients
	LP	NS	MC	LD	
USA: Lukes and Butler (4) .. .. .	16	40	26	18	377
USA: Crum <i>et al.</i> (9) .. .. .	11	32	44	13	167
UK: Gough (10) .. .. .	20	15	29	36	96
UK: Farrer Brown <i>et al.</i> (11) .. .. .	14	56	30	0	50
Germany: Hamann <i>et al.</i> (12) .. .. .	15	41	21	23	508
Denmark: Anderson <i>et al.</i> (13) .. .. .	17	32	34	17	142
Argentina: Braylan <i>et al.</i> (14) .. .. .	13	35	42	8	144
Colombia: Correa and O'Connor, (15) .. .. .	17	12	51	22	102
South Africa: Selzer <i>et al.</i> (16) .. .. .	14	26	35	25	122
Uganda: Wright (5) .. .. .	18	12	50	20	128
Nigeria: Onyewotu <i>et al.</i> (17) .. .. .	12	4	42	42	65
Zambia (present study) .. .. .	16	10	53	21	38

**Table 9**  
*Hodgkin's disease in children*

Source	Histological type								Total cases
	LP No.	%	MC No.	%	NS No.	%	LD No.	%	
Manchester .. .. .	16	30	26	49	6	11	5	10	53
Kenya .. .. .	6	15	16	41	6	15	11	28	39
Tanzania .. .. .	6	17	9	26	4	11	16	46	35
Uganda .. .. .	14	24	17	29	4	6	24	41	59
Zambia (present study) .. .. .	2	15	8	62	1	8	2	15	13

## DISCUSSION

### *Histological diagnosis and classification*

The polymorphic histological appearance of Hodgkin's disease presents many problems in accurate diagnosis. Symmers (18) noted a high rate of misdiagnosis. In our study we also found 7/45 cases misdiagnosed as Hodgkin's disease. This was due largely to inadequate material or poorly preserved tissue. In some cases it was apparent that different criteria were applied by pathologists. Wright (5) found similar discrepancies in Uganda.

The Rye modification (19) of the Lukes and Butler classification (4) of Hodgkin's disease is now generally accepted as being both practical and reproducible. We have adopted this classification in our study. However, several authors still use different classifications (20). Comparison of statistics thus becomes difficult.

### *Incidence*

The age-standardized rates indicate a low incidence of Hodgkin's disease in Zambia. Similar rates have been recorded in Japan, India, Hawaii-Fillipinos (2), and Uganda (5).

The age-specific incidence curves for Hodgkin's disease were generally bimodal, with a peak in young adult life (15-34 years) and another peak in late adult life (after 50 years). Although the pattern varies with geographical location, the bimodality appears to be a constant and characteristic feature of Hodgkin's disease. The bimodal curve was seen in Zambian males. However, there was no peak in young adult life in Uganda (5) and Japan (2). A flat Zambian female curve with a single small peak (40-49 years) was noted even though the female:male population ratio is nearly 1:1.

### *Histological types*

The incidence of different histological types varies in different geographical areas (Table 8). Mixed cellularity was the most frequent histological type observed in Zambia (53%). This was also noted in Uganda (50%), Colombia (51%), Argentina (42%) and U.S.A. (44%) (Table 8).

Nodular sclerosis was an uncommon type in our study and confirmed the observations of others (5, 10, 15, 17). In contrast, it constituted the commonest type in U.S.A. (4), U.K. (11), and Germany (12). No immediate explanation is available. However, it should be noted that even in the same country different authors report different rates for the histological types (4, 9, 10, 11).

Cases of LD with poor prognosis were not infrequent in our study and the histological variants of mixed cellularity and lymphocytic depletion were most frequently observed (74%) in Zambia. This may suggest that our patients came late with advanced stages of Hodgkin's disease (MC, LD). However, Strum and Rappaport (21) in a study of sequential biopsy

material have reported that the histological grades of Hodgkin's disease tend to remain constant over prolonged periods of time.

### *Sex incidence*

Hodgkin's disease occurs nearly twice as frequently in males as in females (6, 14). A high male:female ratio has been noted in Africa by several authors (5, 17). Our observations are similar. The low incidence of Hodgkin's disease in Zambian females was most marked below 30 years (male : female ratio 5.6 : 1).

The incidence of the disease was higher (34%) in Zambian children than reported in Europe (7) and U.S.A. (9). This may be due to the structure of the Zambian population where the majority of the population is younger than in western countries. A male preponderance and high incidence (77%) of MC and LD types with poor prognosis are the features of the disease in Zambian children. Our findings are similar to those reported in East African children (7) and in Lebanon (22). Strum and Rappaport (21) found a high frequency of NS (62.8%) and LP in U.S.A. children. The majority were boys (91%).

### *Aetiology*

Correa and O'Connor (15) postulated three and possibly four epidemiological patterns of Hodgkin's disease varying with socioeconomic standards of the community. They suggested that the differing pattern of the disease in under-developed and developed countries could be explained on the basis of exposure to an infective agent in early life with a defect in host response in communities with poor socioeconomic standards.

MacMahon (23) on the basis of the epidemiological findings suggested that Hodgkin's disease might be several disease entities of differing aetiologies and prognosis presenting at different times of life. He suggested that this could explain the bimodal distribution of the disease in the general population.

Davies (24) suggested that Hodgkin's is a single disease due to an infectious agent or agents and that the histological variants indicate different reactions to a single disease process. Smithers (6) viewed it as a single progressive neoplastic disorder arising primarily in the cell-mediated arm of the immune system, initiated by inherited or acquired defects and by prolonged or aberrant stimulation subject to enhancement by sudden demands resulting from infection or some interference with normal control mechanism.

The almost continuous stimulation by infectious and parasitic diseases, especially malaria, in Zambia must have a profound effect on the lymphoreticular and immune system of the host. Its role in the causation of Hodgkin's is, however, uncertain.

The occurrence of almost an epidemic of Hodgkin's disease (25) with evidence of person-to-person transmission and time-space clustering, seasonal incidence, and certain clinical features strongly suggested a viral aetiology. Order and Hellman (26) have suggested viral transformation of T cells leading to cell-mediated autoimmunity, T-cell depletion, and possibly neoplasia.

The mystery of the exact aetiology of the condition remains unsolved. Our study revealed that it is an uncommon lymphoma in Zambia. As yet the numbers in our study are too small to suggest any common aetiological factor.

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