

Papers and Originals

Geographical Distribution of Cancer in East Africa: A New Clinicopathological Approach

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Geographical pathology is the study of disease-incidence rates in different geographical areas. Comparison may be made between widely separated areas with considerable geographical and economic differences, such as Great Britain and East Africa, or between more closely related countries, such as Uganda and Nigeria, or between different areas in the same country. It is this latter approach that we wish to stress in this article.

In most technologically advanced countries with mobile populations the majority of people live under very similar circumstances apart from specific hazards associated with special industries and individual customs. By contrast, in East Africa there are still many groups of people living in circumscribed communities in different geographical circumstances and exposed to widely varying nutritional, social, economic, and other environmental factors. These groups do not correspond to political boundaries, and from the standpoint of disease Southern Sudan can be regarded as an extension of Northern Uganda ; South-west Uganda is part of the mountainous area containing Kivu, Rwanda, and Burundi (Fig. 1) ;

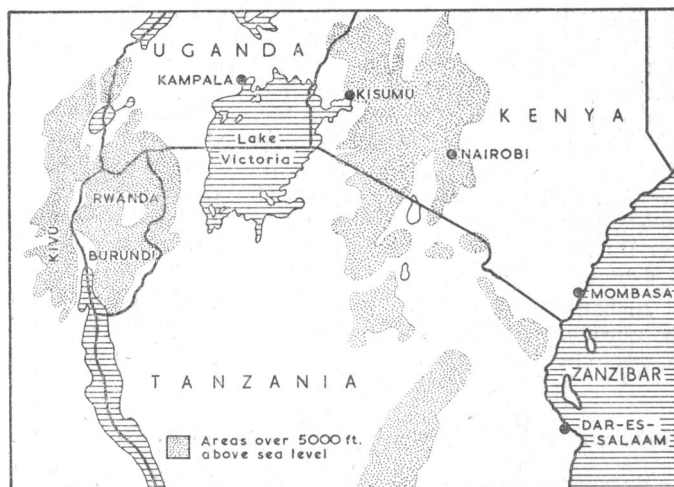


FIG. 1.—Map of East Africa showing main centres and high-altitude areas.

and the coastal plains of Kenya and Tanzania have many more factors in common with each other than with their own inland areas. Similarly, on a tribal basis the Karamajong of Uganda, the Suk of Kenya, and the Masai of Kenya and Tanzania have many more factors in common with each other than with other tribes in the same territory. The Bakiga people of Uganda in turn share more environmental factors with the Banyarwanda than they do with other Uganda tribes. In the study of

geographical factors in any disease process the study of intra-territorial differences must go hand in hand with the inter-territorial and international studies (Burkitt, Nelson, and Williams, 1963).

Methods

The pioneer work of Davies, Wilson, and Knowelden (1958, 1962) has already demonstrated significant differences between the pattern of cancer in the Kyadondo area of Uganda and most Western countries. It has been shown, however, that some tumours do not have a uniform incidence in East Africa. Early in the epidemiological studies on African lymphoma it was observed that this tumour is virtually never seen in the densely populated high area of South-west Uganda. Dodge, Linsell, and Davies (1963) have also shown marked differences between the incidence of cancer of the penis in Uganda and in Kenya, and related this to differences in the custom of circumcision between Ugandan and Kenyan tribes.

These facts led us to wonder whether other tumours may show marked differences in incidence in East Africa and surrounding countries.

In 1963 we decided to start a new approach to the cancer situation to try to fill in some of the gaps in our knowledge of the cancer pattern in East Africa, particularly in Uganda.

The first step was to open up the diagnostic histology service to all hospitals in Uganda, and to encourage biopsies, particularly of selected tumours. This was aided by the use of biopsy bottles containing neutral formalin prepackaged together with request forms requiring details of age, sex, tribe, and habitation, similar to those used by Davies *et al.* (1958) for the Kyadondo survey. As a result of this step the overall biopsy rate went up from 4,500 in 1962 to 6,900 in 1964. All histologically proved cases of cancer from Uganda are now registered, and 1,500 new cases were recorded in 1964. Fortunately, while valuable for research, this operation is still more valuable as a link between outlying doctors and the university centre, and is much appreciated for this reason as well as for the practical service offered.

The second step was to establish direct contact with the doctors in all the hospitals in Uganda, and in most of Kenya and Tanzania, to acquaint them with the scheme, to encourage biopsies, and particularly to obtain routine returns providing particulars of certain selected tumours. During these visits the opportunity was taken to probe into the experience of the local doctors, and to examine returns and operation records with a view to establishing some ideas of certain cancer frequencies. In East Africa there are a number of mission hospitals that have doctors who have served them for over 10 years and not a few for over 20 years. This staff continuity means not only that impressions of incidence have been formed over many years but

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also that an added interest in accurate records has in many instances led to careful recording of cancer and other figures and to the establishment of miniature cancer registries.

Several mission hospitals in East Africa have been keeping careful records of their cases of cancer, and these have provided valuable information. Thus Dr. Joe Taylor (1964), at the "Jungle Doctor" Hospital at Mvumi, in Tanzania, was able to compare experience at that hospital with the review of the Mengo Hospital experience recorded by Davies, Elmes, Hutt, Mtimalvalye, Owor, and Shaper (1964).

Discussions with many clinicians and examination of existing records, during extensive travel, have led to the emergence of some cancer and other disease patterns throughout East Africa which supplement the more detailed and accurate results for Uganda recorded in the Cancer Registry. These are being followed up through the biopsy service and regular returns.

Results

In this paper we are concerned with outlining our general methods of geographical study in Africa and reporting some preliminary observations. The latter can be divided into the factual information derived from the Cancer Registry for Uganda and the general impressions obtained from visits and postal communication with adjacent countries.

In the Table are shown the percentage incidences of selected tumours from different areas of Uganda (Fig. 2) for 1964,

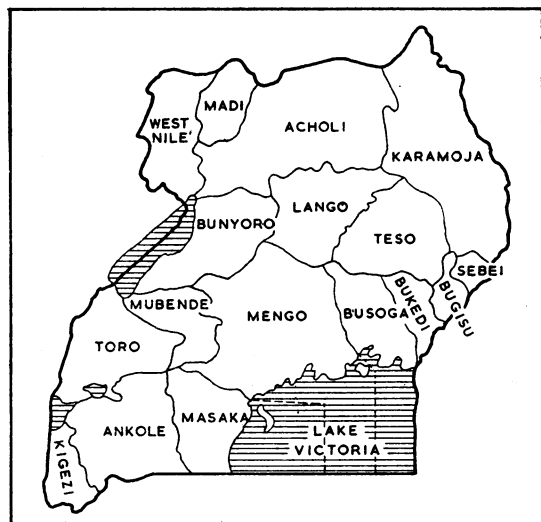


FIG. 2.—Map of Uganda showing districts.

together with the number of cases and the total returns from the area. The regions chosen for comparison had all been visited by us before 1964, and biopsies had been encouraged and facilities made available. All the hospitals in each region were included in the scheme. The Table shows the fallacy of expressing returns for individual tumours from the whole country as a percentage incidence. Selection of the tumours for this preliminary report was based on the fact that they were easily diagnosed clinically and accessible to biopsy. Moreover,

they were relatively common, and verbal reports had suggested different incidence rates in various areas of East Africa.

Cancer of the Penis

The lower incidence of this tumour throughout most of Kenya has been reported by Dodge *et al.* (1963). In contrast to Uganda the majority of tribes practise circumcision, and penile cancer is prevalent only in the western part of the country, chiefly among the uncircumcised Luo. These authors also noted considerable differences between uncircumcised Ugandan tribes, and these differences have been confirmed by Kyalwazi (1964). These reports are borne out by our returns for 1964, which show that cancer of the penis accounts for 17% and 20% respectively of all malignant tumours in Teso and Bunyoro, whereas in Lango and West Nile/Madi the figures are only 1.4% and 0.0% (see Table). We have discussed these differences with good clinicians who have spent several years in these areas, and the differences bear out their experience. As none of these tribes circumcise it is evident that secondary factors must be vital in the production of carcinoma; it is hard to believe that there were significant differences in social hygiene between these groups, and further studies will be necessary to elucidate factors such as infection (Ntuyabaliwe and Mluge, 1965).

There is no significant relation between the incidence of carcinoma of the penis and carcinoma of the cervix. For example, the Cancer Registry returns for 1964 show that, whereas in Lango there were nine cancers of the cervix to one of the penis, in Teso there were nine cancers of the cervix to 16 of the penis. In Zanzibar (Chopra, 1964) cervical cancer is the most frequently observed cancer, though cancer of the penis is unknown.

Kaposi's Sarcoma

This tumour is relatively common throughout East Africa, accounting for about 4% of all malignant tumours. The cancer registry figures for 1964 suggest that the disease is more common in the west, particularly the north-western area of the West Nile and Madi, where it accounts for 18.2% of all registered tumours (see Table). This area abuts on to the North-east Congo, from where the highest incidence in Africa has been recorded (Oettlé, 1962). A high incidence of Kaposi's sarcoma has also been observed in Rwanda and in Eastern Kivu, both of which form part of the Western and South-western borders of Uganda (Gigasse, Clemmeson, and Maisin, 1962). This observation was recently confirmed by one of us (D. B.) during a visit to all Rwanda hospitals and the Central Laboratory at Butare.

In both Kenya and Tanzania Kaposi's sarcoma appears to be uncommon on the coastal plains (Slavin, 1965). Zanzibar seems to be almost exempt, only one case having been recorded.

Squamous-cell Carcinoma in Tropical Ulcer Scars.

By contrast with Kaposi's sarcoma the incidence of malignant change in tropical ulcer scars appears to be very low in the north-west (3.6%) and to have a focus of very high incidence

Kampala Cancer Registry, 1964

	Bunyoro. Toro	Ankole	West Nile/Madi	Lango	Bukedi. Bugisu. Sebei	Teso	All Uganda
Breast	3.3% (2)	5.2% (4)	3.6% (4)	4.2% (3)	4.3% (5)	7.4% (7)	4.6% (68)
Penis	20.0% (12)	3.9% (3)	0.0% (0)	1.4% (1)	7.7% (9)	17.0% (16)	7.5% (110)
Squamous-cell carcinoma of skin ..	5.0% (3)	12.0% (10)	3.6% (2)	21.0% (15)	14.5% (17)	9.6% (9)	7.0% (103)
Kaposi sarcoma	6.6% (4)	6.5% (5)	18.2% (10)	2.8% (2)	3.4% (4)	3.2% (3)	4.2% (61)
Burkitt's tumour	0.0% (0)	1.3% (1)	18.2% (10)	8.5% (6)	5.1% (6)	5.3% (5)	4.3% (63)
Total No. of registered cases ..	60	77	55	71	117	94	1,463

Percentages refer to the incidence of a particular tumour relative to the total in each area.

in Lango (21.0% of all tumours) (see Table). Ntuyabaliwe and Mluge (1965) and Shepherd (1965) have drawn attention to the low incidence in people of the Baganda tribe.

Burkitt's Tumour

Over 500 cases of this tumour have now been recorded in Uganda. Less than 4% have come from the south-west, most of which is at an altitude of over 4,500 ft. (1,370 metres). Over 20% of the population of Uganda live in this region.

Breast Cancer

No significant differences in incidence have been observed.

Hepatoma

The tumour is common throughout the area under consideration, and an attempt is being made to obtain better returns from up-country by the encouragement of liver biopsy, both in life and at necropsy. Eighty-one cases were registered in Uganda in 1964, forming 5.5% of all malignant tumours. The only unusual finding was that six cases were recorded in Karamoja, which is thinly populated by nomadic herdsmen. In relation to the overall returns from this area it is a very high incidence. In view of the suggested relationship between primary liver cancer and *Aspergillus flavus* it is interesting to note that these people live mainly on blood and milk, although they do also store grain crops.

Preliminary impressions outside Uganda suggest that the tumour has a very high incidence throughout the central plain of Tanzania, where in several hospitals it was said to be the most frequently observed cancer.

Cancer of the Stomach

Davies (1959) has pointed out the low incidence of gastric cancer in the Kyadondo area of Buganda, and most figures from other parts of Africa confirm this. However, throughout much of Rwanda the condition is thought by many experienced doctors to be one of the commonest neoplasms. In Eastern Kivu, which is topographically an extension of the Rwanda hills into the Congo, Ceuterick (1960) and Gigasse *et al.* (1962) have produced convincing figures that suggest a very high focal incidence in these areas. There also appears to be a high incidence in North-west Tanzania (Nillroth, 1964; Bundschuh, 1964).

In a recent analysis of the tribal distribution of certain tumours based on the Kampala Registry Mati and Auma (1964) reported a comparatively high incidence in Banyarwanda living in Uganda and in the Banyankole from the south-west adjacent to Rwanda. The tumour appears to be particularly rare in Northern Uganda. Williams (1965) has seen only one case in a series of 222 malignant tumours recorded in Kuluva Mission Hospital, and De Souza (1965) has not seen a single case during the two and a half years as surgeon in the busiest surgical unit in the northern region.

Cancer of the Oesophagus

Within East Africa great variations in incidence of oesophageal cancer are observed. There appear to be two areas of unusually high incidence, in contrast with other areas where the disease is not recognized.

Several workers, and in particular Miller (1964), Nevill (1964), and Clifford (1964), have drawn attention to the local concentration of this disease around Kisumu on the north-east

shore of Lake Victoria. Ahmed (1965) has studied this problem in detail. He is recording approximately 40 cases a year with histological confirmation at Kisumu Hospital. This is more than double the total cases recorded at Mulago Hospital in Uganda, which contains four times as many beds and is the referral centre for all Uganda. Three mission hospitals within 50 miles (80 km.) of Kisumu estimate that oesophageal cancer is their most frequently observed neoplasm. At the next provincial hospital, less than 100 miles (160 km.) to the east, da Cunha (1965) reports that most of the cases referred to him have come from the Kisumu area.

A second area of high concentration is apparent in the vicinity of Mount Kenya. The provincial hospital situated at Nyeri to the west of the mountain receives referred cases from all this area and records an estimated 10–15 oesophageal cancers annually. There is some evidence suggesting that the majority of these patients come from the east of the mountain, where two mission hospitals with 100 and 150 beds respectively see an estimated 10–15 cases a year each.

In contrast to these two areas of high incidence of oesophageal cancer no doctor throughout Rwanda could remember having seen a single case, and Williams (1965) has recorded no case in his 24 years in Northern Uganda. Gigasse *et al.* (1962) recorded the apparent absence of oesophageal cancer in Eastern Kivu, which is topographically only an extension of Rwanda. The tumour also appears to be very rare in the areas of South-west Uganda and Western Tanzania adjacent to and topographically identical with Rwanda.

Discussion

It is evident that in East Africa significant variations of incidence in certain cancers can be observed between areas closely related geographically. The clarification and confirmation of these emerging patterns should provide an opportunity to search for environmental factors common to areas showing a similar incidence or differing between areas of high and low incidence.

Much information has already been obtained by analysis of central laboratory histological records. In the three East African countries all histology has been done for many years in laboratories in the capital cities. Figures for cancer incidence based on these central records, while giving a general pattern, may be very misleading if they are not analysed on a local geographical basis. Furthermore, the returns from different parts of the country show a great variation. The most accurate and valuable figures so far obtainable have been derived from the Kampala Cancer Registry survey of Kyadondo country (Davies *et al.*, 1958, 1962). It is evident, however, that while surveys of very localized areas such as Kyadondo will produce more accurate figures they will miss the variability that we know exists even in such a small area of Uganda.

It is considered essential that a combined clinicopathological approach be made to this problem. Active co-operation from clinicians is an essential preliminary to the provision of biopsy material, and this can best be achieved after initial personal contacts. On the other hand, only histological confirmation can provide the accuracy of diagnosis without which purely clinical diagnosis can always be open to doubt. Initially, investigations must be limited to a selected small group of tumours such as those discussed in this paper.

It is as true in medicine as elsewhere that you see what you look for. The absence of a condition in an area, which may be more significant than its high incidence, can be determined only if observers are specifically looking for it. An active search can be maintained by any one individual for only a limited number of conditions.

Although this paper has been limited to the geographical study of cancer, this combined clinicopathological approach

has gleaned information which indicates that several non-neoplastic conditions exhibit even more striking patterns of distribution which warrant further study.

The statistical purist may well comment that figures for cancer incidence based on such evidence are useless. We do not believe this to be true, and we feel that in an area such as this every factual piece of knowledge is of value.

Summary

Carcinoma of the penis, Kaposi's sarcoma, squamous-cell carcinoma of the skin, oesophageal cancer, and gastric carcinoma have a variable incidence in different parts of Uganda and probably in other areas of East Africa. General statements about cancer in Africans should therefore be accepted with reserve. More accurate figures are needed before studies on aetiology can be started. These figures may be attained by a combined approach on the part of the clinician and pathologist. Personal contact is an essential feature of such a programme.

Our thanks are due first to the Ministries of Health of Uganda, Kenya, Tanzania, and Rwanda for their permission to make these safaris and to visit Government hospitals. We would also like to thank all the doctors in both Government and Mission hospitals throughout East Africa for giving up valuable time to discuss their work. Finally, we would like to thank all our colleagues in the New Mulago Hospital and the Makerere University College Medical School for their help, advice, and co-operation. We would also like to acknowledge our debt to Professor J. N. P. Davies, who initiated this type of work in East Africa.

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Aetiology and Management of Bronchiolitis and Pneumonia in Childhood

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In presenting our observations on bronchiolitis and pneumonia in children admitted to Newcastle upon Tyne hospitals during the winter of 1963-4 we are concerned with four problems.

1. *Part Played by Viruses.*—Infection with respiratory syncytial virus (R.S.V.) is now accepted as a common cause of acute disease of the lower respiratory tract, and our experience is in agreement with this (Chanock *et al.*, 1961; Reilly *et al.*, 1961; Adams *et al.*, 1961; Holzel *et al.*, 1963; Andrew and Gardner, 1963). It is not the only virus involved, and there are a substantial number of acute respiratory illnesses from which no infective agents have so far been isolated. More information is needed about the relative importance of the different viruses in different parts of the country in different years, and we felt that our experience in 1963-4 should be recorded.

2. *Extent and Significance of Bacterial Infection.*—A clear understanding of this subject is necessary if antibiotics are to be used rationally, but facts are few, and the conclusions of different workers contradictory. The main obstacle is the difficulty of obtaining, by methods suitable for routine use, specimens which

give reliable information about the bacteriological condition of the lower respiratory tract, particularly as the answers obtained are distorted through children having received antibiotics before coming to hospital. The increasing importance of *Staphylococcus aureus* as a cause of pneumonia in infancy is well known. While assessing the contribution of this organism we felt it was also necessary to consider the claim by Wood *et al.* (1954) and Sell (1960) that capsule strains of *Haemophilus influenzae* are responsible for bronchiolitis.

3. *Causes of Death.*—In England and Wales in 1962, 2,944 children died from "bronchitis and pneumonia," bronchiolitis being included in this total and not listed separately (Registrar-General, 1963). These were one-sixth of all the deaths in childhood and one-quarter of those occurring after the first week of life. Yet, in many articles published in the past 10 years, accounts of the pathology in children who died are lacking or incomplete.

4. *Rational Management of Children with Bronchiolitis.*—The extent to which management is rational will depend on how far we understand the full effect of the virus infection, the extent of bacterial intervention, and the disturbance of pulmonary function and other systemic disorders to which they give rise. In all these aspects knowledge is incomplete, yet no carefully controlled trials of the many remedies in common

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