

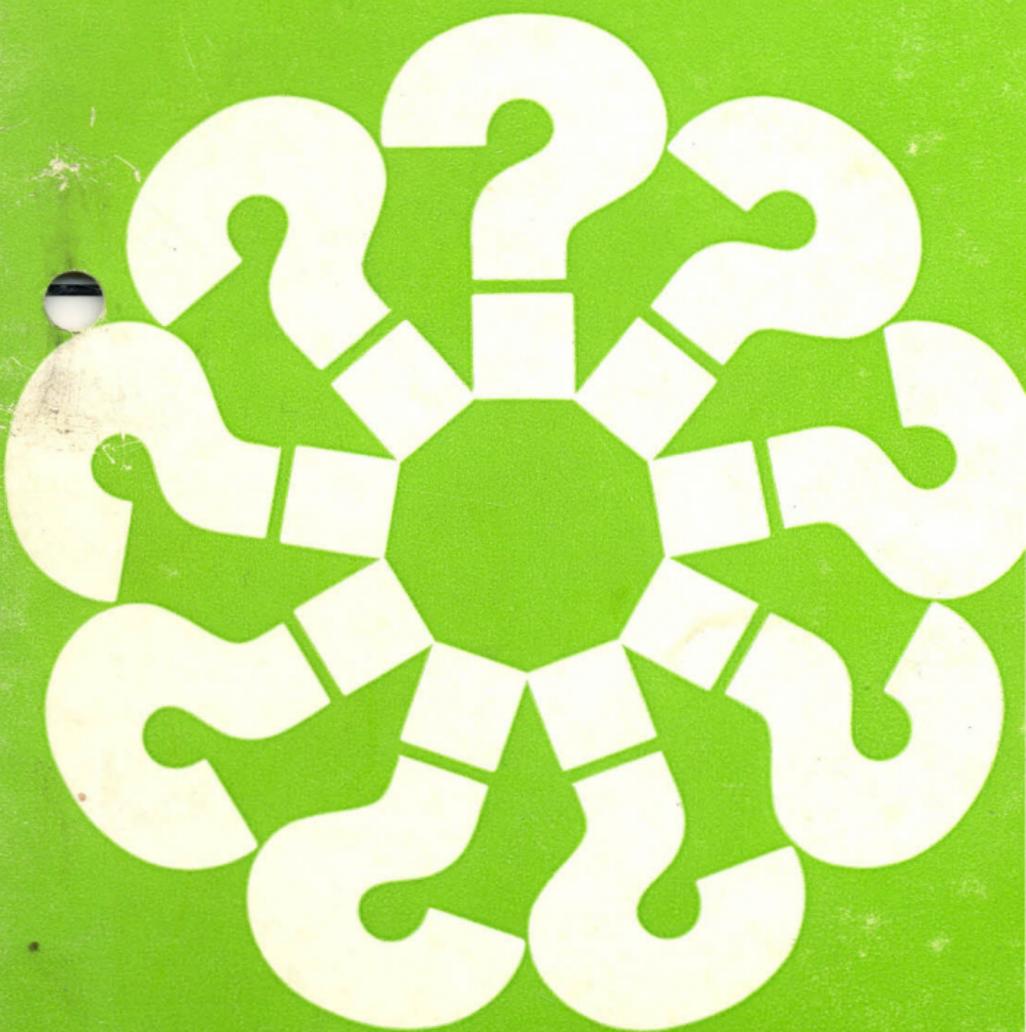
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KENYA'S CANCERS

CHANCELLOR
NAIROBI



THE INAUGURAL LECTURE SERIES was started in the days of the University of East Africa when it was a tradition of the then University College Nairobi to have its newly appointed Professors deliver their first public Lecture in Nairobi. The University of Nairobi has now started their new series of Lectures and in an attempt to have these memorable lectures well documented and preserved, the University Deans' Committee has granted funds for its publication. This is the first of such a series and will be available on sale at bookstores.

Cancer is a world-wide problem, but its distribution shows marked geographic variations. This is particularly evident in Africa where some tumours are found to be very common in certain areas. It is probable that this indicates the presence of cancer-producing factors in the environment, and in Africa there is an opportunity to investigate this relationship. Already, notable advances have been made in implicating a virus as a cause of the childhood tumour, Burkitt's lymphoma; current research points to the possibility of a chemical cause for cancer of the oesophagus which is particularly common in Nyanza; and both viral and chemical causes may be involved in the common cancer of the liver.

These three cancers are selected from the tumours which are commonly seen in Kenya, and Prof. Hector M. Cameron dynamically illustrates the probable role of the environment in their genesis.



Hector M. Cameron

Professor Cameron was appointed Senior Lecturer in Human Pathology in the Nairobi Medical School in 1967, and a year later became the first Professor of that Department. He came on secondment from the Royal Infirmary, Glasgow, where he held appointments as Consultant Pathologist and Honorary Lecturer, and was responsible for the diagnostic histopathology service and participated in undergraduate and postgraduate teaching.

His research interests are in liver disease, tumour pathology and deep fungal infections.

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KENYA'S CANCERS

Visitors to East Africa are commonly taken aback by the wealth of novel experiences that thrust upon them and, in attempting to describe them, all too often fall back on the well worn phrase "Ex Africa semper aliquid novi", which, I believe, was novel in the time of Pliny. In spite of its venerable age, this is a truth which the newcomer cannot ignore — yet it is only a partial truth: What is perhaps more impressive to the medical immigrant from the west is that Africa can duplicate most of the disease processes found in the Old World, and may present familiar conditions in new and surprising lights; almost as though it were saying "anything you can do I can do better". There are many myths and misconceptions about disease in Africa, and one contribution the newcomer may make is to look at the field with eyes undimmed by such preconceived ideas; he may then, if he is fortunate, identify conditions which tradition maintains do not occur here. Of all the conditions which tradition formerly excluded from Africa, perhaps the commonest is cancer, and it is largely through the patient work of regional cancer registries such as those in Kampala and Nairobi that a more accurate picture has been formed, and we now know that cancer poses major problems of patient care and presents immense opportunities for research. Davies, who established the Cancer Registry in Kampala, showed that overall incidence rates are in fact similar to those reported from Europe and North America, at least, up to middle-age; thereafter, because of the shorter expectation of life in African countries, the incidence falls.

It is understandable in countries where the main killing diseases are infective and parasitic, that cancer should be overlooked. Occasional cases of cancer are overshadowed by the hosts of patients suffering from pneumonia, tuberculosis, measles, amoebiasis, schistosomiasis and malaria, to name a few of the common lethal diseases. It is not surprising that, in the presence of so many conditions which are either preventable or curable, there is some impatience with those who choose to turn their skills to the more intractable and, in statistical terms, less important problems of cancer. The history of cancer research in the last seventy years gives substance to such objections. This century has seen the expenditure of vast

sums of money and the devotion of endless hours of highly skilled and sophisticated research into cancer; yet we are still remarkably ignorant of the processes which control normal cell growth and differentiation, and of the basic differences between a normal cell and a malignant one. Why then impose on Africa, with all its more pressing problems, such a vast and knotty problem? The only justification I believe is that Africa presents clues which are not to be found in the technologically advanced countries of the world. These clues point firmly to the environment as being of major importance in the causation of cancer. Many observations show quite dramatic geographical variations in the incidence of various forms of malignant disease. Burkitt's lymphoma is the commonest form of cancer in children over large areas of sub-Saharan Africa, yet is hardly known in other parts of the world; carcinoma of the oesophagus is the commonest tumour of men in West Kenya, and carcinoma of the liver may be fifty times as common in Africa as in Europe. The potential for this type of epidemiological investigation is well illustrated by developments in the investigation of Burkitt's lymphoma. Although, it is only thirteen years since Denis Burkitt first described this tumour and its distribution, more advance has been made in that time into an understanding of its nature and pathogenesis than I imagine into any other internal cancer in the past fifty years. This surely is one of nature's great experiments which opens the door to further advances which will be of significance far beyond Africa. I propose to use these different cancers to illustrate current thinking on ways in which the environment may be of importance in the genesis of cancer.

Cancer and the environment.

In viewing any of these tumours as possible products of the environment, one must stress that environment is a wide and nebulous concept, but in the sense I am using, it embraces any factors emanating from outside the body. Thus it includes substances in the air we breathe or in the food we eat, microorganisms—bacterial, viral or parasitic—and physical stimuli such as ultra-violet and atomic radiation. In Europe and America, pollution of the environment is understandably becoming an object of public concern; it is commonly — and

I believe mistakenly — assumed that most harmful substances in the environment are put there by man himself. This is a belief which is easy to understand when one has witnessed the appalling pollution of the air over large industrial cities, or a once clean river turned into a sewer. Perhaps as a reaction to this, it is sometimes held that anything which is natural and unspoiled is by definition pure and health-giving, whereas, when the nest is fouled, man himself is responsible. In Kenya and similar countries, we have an opportunity to test this hypothesis. Here, in spite of the vast and accelerating social and cultural changes since Uhuru, we have a relatively stable society, predominantly rural and for the main part exposed to fairly constant environmental conditions in which it is possible to examine the environment for noxious influences and to attempt to relate these to disease processes. This is more difficult than in the common bacterial diseases, in which case-to-case infections may be obvious and the incubation period is short; in cancer, the incubation period is long, possibly covering many years. However, such a search has more prospect of success in Africa than in the technologically advanced countries with their indiscriminate mixture of social, cultural and ethnic backgrounds.

Since the start of this century there have been two main objects of investigation as possible causes of cancer—chemical carcinogens (cancer-producing substances) and viral causes. Solar and x-irradiation were incriminated early because their role was more immediately obvious and could readily be investigated experimentally. Interest in chemical carcinogens was aroused by observations on industrial skin cancers, apparently resulting from prolonged contact with soot, tar and oily substances. The possibility that internal cancers might also be caused by chemical substances was suggested by the finding of a high incidence of bladder cancer in workers in the rubber and aniline dye industries. This opened up a vast field of investigation and there are now hundreds of compounds known to be carcinogenic in experimental animals. Many are common in nature but their role in producing human cancer is quite undecided. It is, of course, not possible to extend the animal experiments to man, but I will attempt to show that by looking for naturally occurring carcinogens in relatively stable communities with a high incidence of a particular

tumour, it is possible to pick up some promising clues.

While interest in chemical carcinogens has been a constant feature of cancer research over the past half-century, the popularity of viral carcinogenesis has been much more variable. Peyton Rous described his sarcoma in chicks in 1910, and twenty years later Shope produced viral papillomas and skin cancers in rabbits. Also in the thirties, Bittner found a "milk factor" now known as the mammary tumour virus which was associated with cancer of the breast in mice, and since then viruses have been implicated as the cause of a number of leukaemias in experimental animals.

It is strange that, after the first excitement over the early discoveries at the beginning of the century, many doctors seemed to lose interest, and research into viruses in cancer became the esoteric field of a small group of scientists, very often with little relation to clinical medicine. Human cancer was suddenly and dramatically brought back into the picture by the discovery of Burkitt's lymphoma and the epidemiological studies which suggested a viral cause.

Before going on to describe my three chosen cancers, let me give a little background information on cancers in Kenya.

The Kenya Cancer Registry, which was established by Dr. Linsell of W.H.O. attempts to register all cases of cancer diagnosed in any part of the country; at present this runs at over fifteen hundred cases per year. As a rough guide, we can express the frequency of any single tumour as a proportion of all cancers (Table 1). Clearly, this

SOME COMMON CANCERS IN KENYA.

Table 1

	1967 — 1970	% of Total
All cancers	5,943	100
Carcinoma of Skin (Scar Cancers)	551	9.3
Carcinoma of Cervix	480	8.1
Hepatoma	353	5.9
Carcinoma of Oesophagus	336	5.7
Melanoma	227	3.8
Nasopharyngeal Carcinoma	207	3.5

is influenced by the distribution of medical facilities, the interest and enthusiasms of medical staff, and the readiness with which the local populace

seeks medical assistance. Such factors may easily lead one into interpretative errors, but in the absence of adequate demographic data and a uniformly competent health service, it is the best indication we have. In fact, provided the hazards are borne in mind, useful observations can be made. It shows that carcinoma of the liver, which accounts for about 6% of all malignancies, comes third in the table of frequencies of cancer in Kenya. It is a long way behind the more accessible and easily diagnosed squamous carcinoma of the skin which is responsible for about 13% of the total, and is also less common than carcinoma of the cervix of the uterus which is just over 8%. Carcinoma of the oesophagus comes fourth in the list, but its main interest lies not so much in its overall frequency as in its uneven territorial distribution within Kenya and in relation to neighbouring countries. Some forms of cancer which are very common in western countries — notably carcinoma of the lung and carcinoma of the colon — are quite uncommon in East Africa. One may take this as negative evidence in favour of environmental influences. Cigarette smoking, which is now established as the major cause of lung cancer, is a relatively recent phenomenon here, and is still a much less common indulgence than in Europe or America. I do not doubt that, as it gains in popularity, it will be paid for in the lives of men. The reasons for the dearth of cases of carcinoma of the colon are not established, but there is evidence that it may be related to the high residue diet of Africans which leads to a rapid emptying of the bowel. Very little attention has been given to the possibility that bowel contents might contribute to the aetiology of cancer of the bowel, and this possibility has now been proposed, not as a result of studying the disease in countries where it is common, but by contrasting it with the African situation where it is uncommon.

Returning to tumours which are common in Kenya, let us first look at the one which has gained prominence because of the possibility that it is caused by a virus — Burkitt's lymphoma.

BURKITT'S LYMPHOMA

This is a childhood cancer, in which the tumour consists of malignant lymphoid cells. It is similar microscopically to another malignant tumour — the lymphosarcoma — which is found in all parts

of the world, but it has notable distinctive characteristics:—

- (a) it is essentially a tumour of children, with a peak incidence between four and seven years; only 5% occur over the age of twenty years.
- (b) it has a peculiar anatomical distribution in many organs of the body, and a particular predilection for the jaws, in which it may form multiple masses. (Fig. 1).

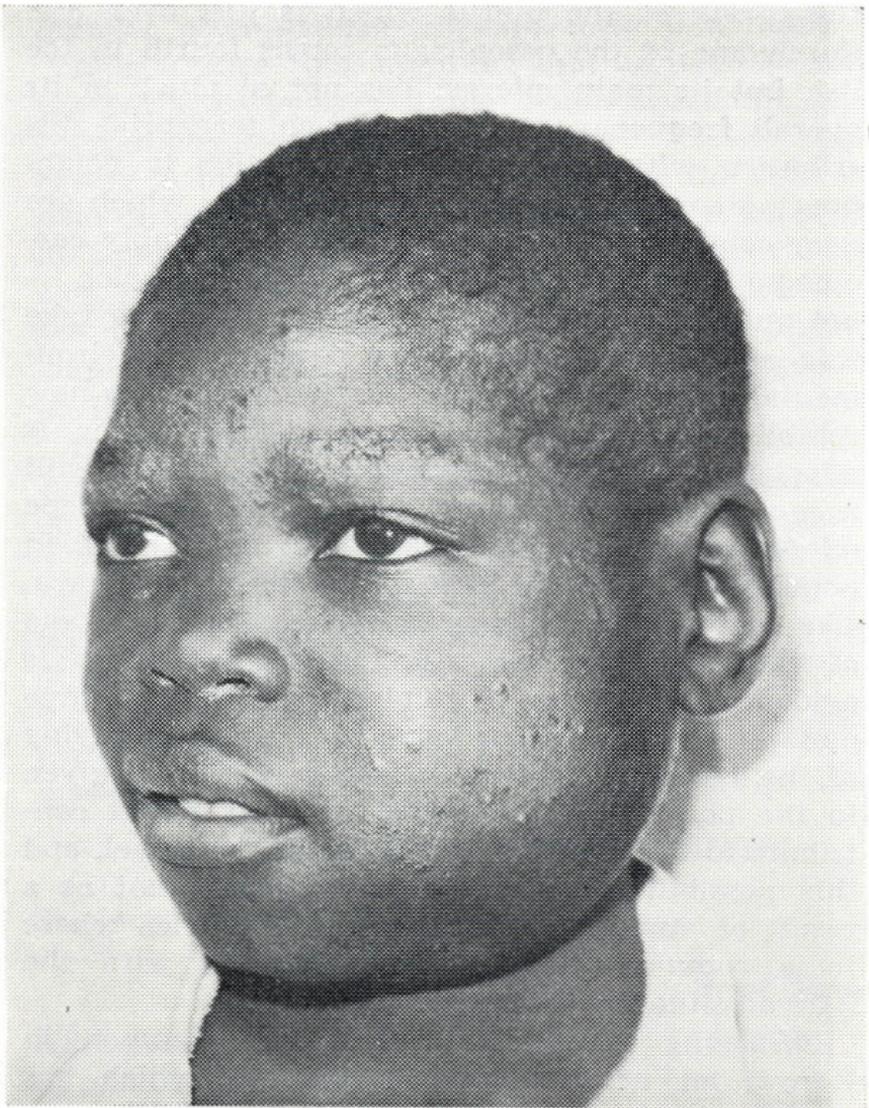


Fig. 1. Burkitt's Lymphoma affecting the left jaw.

- (c) it has a peculiar geographical distribution, being found in a belt across the continent of Africa, between latitudes of approximately 15° north and south of the equator

(Fig. 2). This covers most of sub-Saharan Africa except Rhodesia, Zambia and most of South Africa. It is also endemic in New Guinea and is found sporadically in other parts of the world, including non-tropical areas.

THE 'LYMPHOMA BELT'

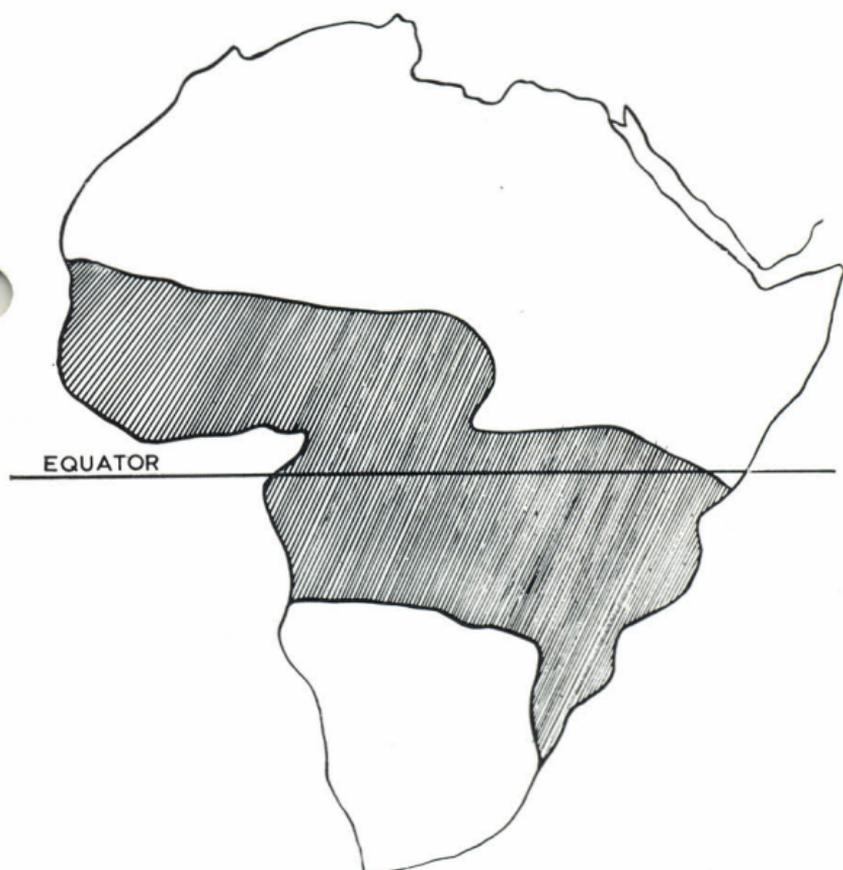


Fig. 2. Distribution of Burkitt's Lymphoma in Africa.

Although it was not defined until the pioneer work of Denis Burkitt in 1958, it can be identified in earlier medical records, and the first clear case was described in 1904 by the first medical missionary to Uganda, Dr. Albert Cook, in the records of the Mengo Hospital.

Most of the epidemiological work has been carried out in East Africa and stems directly from the acute observations of Mr. Burkitt, who identified the disease while working as a surgeon in Kampala. He carefully mapped its distribution on the basis of information received in response to questionnaires and extensive safaris, and found it was mostly confined to altitudes below 5,000 feet, with an annual rainfall of at least 20 inches, in places where the coolest temperature was greater than 16°C. The correlation with minimum

temperature and rainfall is impressive and is reflected in the fact that the altitude barrier becomes lower as one travels away from the equator; it is less than 1,000 feet when one reaches Mozambique. Conversely, the mountainous lands of Ethiopia, Rwanda and Burundi are virtually free of the disease. Davis and Haddow noticed that the map showing its distribution corresponded closely with the map of yellow fever, and for some time there were high hopes that the causative agent might prove to be a virus carried and transmitted by some insect. However, there were anomalies in its distribution; it is absent from some tropical areas which seem to provide all the appropriate conditions, and, on the other hand, sporadic cases are reported from non-tropical countries. For these and other reasons, it had to be accepted that this was not a simple vector-borne virus disease.

However, the evidence was strongly in favour of an infective element and the possibility of this being viral became more likely when virus particles were found in tissue culture preparations of the tumour. Several viruses in fact have been identified, but the one most commonly demonstrated is a herpes-type virus, known as the Epstein-Barr (or E.B.) virus. Not only can this be found in tissue culture preparations of the tumour, but high titres of antibodies to the virus can be identified in the sera of patients. This virus is of world-wide distribution and in fact is probably the cause of infectious mononucleosis better known among American undergraduates as "the kissing disease". If one assumes that it does play a pathogenic role in Burkitt's lymphoma, one has to face the problem why it should cause a self-limiting inflammatory disease in young adults of countries such as America, and a lethal cancer in African children. There is little doubt that in the lower socio-economic conditions of the latter, African children are exposed to the virus at a much earlier age. Furthermore the children who develop the lymphoma live in areas where malaria is holo-endemic (that is, more than 75% of children between the ages of two and nine years show evidence of malaria). Malaria has profound effects on the reticuloendothelial system which is responsible for the body's immunological defences, and the current hypothesis is that a virus — possibly the Epstein-Barr virus — is the causative agent but that it produces its oncogenic (or cancer-

producing) effect in children whose reticuloendothelial systems have been undermined by repeated malaria. In this connection, it may be noted that adult immigrants moving into an endemic area from a Burkitt-free area are as vulnerable as the children of the area into which they move. In Uganda, people who have moved from the tumour-free highlands in the south west, form 20% of the population of Buganda. They produce a considerable number of adult cases; 26% are more than 30 years. This is a familiar phenomenon in other infections, where early exposure results in early disease or active immunity, and late infection produces a crop of adult cases in a non-immune population.

Further evidence of an infective aetiology is provided in detailed studies in the West Nile district of Uganda where most of the cases occurring in a given year tend to occur in one part of the country. A very recent study of such time-space clustering was carried out in Bwamba county in West Uganda and produced five cases over six months in this one area, from which no examples had been reported in the past; two of these were full siblings living in the same house. Such evidence on a small scale supports the large scale epidemiological work pointing to an infective cause and, together with the electron-microscopic and serologic data point to a viral cause for this strange lymphoma.

CARCINOMA OF THE OESOPHAGUS

Our next tumour is a quite different type of cancer — carcinoma of the oesophagus — and, in describing it, I will summarise current work on possible chemical causes.

Carcinoma of the oesophagus or gullet, is a malignant growth arising from the mucosa of the oesophagus and, because the oesophagus is a narrow tube, it readily becomes obstructed and the patients are unable to swallow and become wasted. On a world scale, there is no common tumour which has a more variable incidence from place to place. The Transkei seems to have the world's highest incidence, and here, it is probably around a hundred times as common as in Ibadan or Europe. In Kenya it is also common, particularly in the West around the Kavirondo Gulf where it accounts for 20-25% of all malignant tumours. The Xhosa in the Transkei can recognise the disease and have their own name for it; a disease

must be of frequent occurrence before it acquires a local name. This has also happened in West Kenya where in Kisumu it is known as "duol modinore" (can't swallow). The contrast with neighbouring areas may be quite sharp, there being steep gradients in incidence between one area and another. In East Africa, we see the strange phenomenon of a disease which seems to be controlled by political boundaries. Just across the Western and Southern borders into Uganda and Tanzania, cancer of the oesophagus is found to be of low frequency. In West Kenya, the focus of high frequency is found in an area approximately 150 miles across; yet in Eastern Uganda, less than 100 miles from Kisumu, it is seldom seen.

Such dramatic geographical variations suggest some environmental factor in the genesis of this tumour, and this suspicion is strengthened by the fact that the disease affects two ethnically distinct tribal groups, the Luo and the Muluha.

Estimates of tumour incidence in countries with inadequate, widely scattered medical facilities are inevitably hazardous, and to judge whether a tumour has become more common over a period of twenty to thirty years may be little more than guess-work. Nevertheless, there are some medical centres which have been in existence for this period of time and the changes in frequency are so dramatic that one may accept that there has been a genuine increase. In Johannesburg in the nineteen-thirties, carcinoma of the oesophagus formed 2% of all malignancies; in the nineteen-sixties it was 28%. The tumour was virtually unknown in the Transkei in the thirties; now this appears to have the highest frequency in the world and more than half of all cancers in men are carcinoma of the oesophagus. In West Kenya, the reported increase has been more modest; from 13% to 22%, and this could be accounted for by improved diagnostic services.

The sexes are not equally affected; as in many forms of malignant disease, it is men who are more commonly affected. However, this varies greatly from one part of the world to another. In Kenya, men are eleven times more vulnerable than women. Twenty years ago, the same was true in Johannesburg, but now women are catching up, and in the nineteen-sixties, the male to female ratio was 5:1. In the Transkei, the men are only slightly more affected than women.

The existence of wide variations in the frequency of human tumours, accompanied by the probability that there has been a recent increase, is taken to indicate an environmental cause for this tumour. The male predominance may mean that women are constitutionally less susceptible or else that they are in some way protected from the pathogenic agent, possibly by cultural habits.

One very interesting observation is the occurrence of carcinoma of the rumen and oesophagus in the cattle of a group of Maasai in the Nasampolai valley of the Mau Escarpment in Kenya. This is associated with grazing in high forest clearings, and according to the Maasai the incidence rises in periods of prolonged drought. It also occurs in healthy stock introduced into the valley. The disease is not found in sheep and goats which graze on the valley floor, but since the Maasai maintained that the same condition occurred in forest hogs, two hogs which were seen to be ill, were speared and proved to have carcinoma of the oesophagus.

In searching for the supposed pathogenic agent, the field is dauntingly wide. Medical investigators, who seem to have a Calvinistic streak in their souls which causes them to suspect apparently innocent pleasures, have singled out alcoholic drinks for special attention. In general, it has been found that consumption of alcohol is higher in patients with oesophageal carcinoma than in control groups, but this is true of other conditions, and it seems clear that there is no direct relationship to either quantity or strength of alcohol imbibed. However, investigation of the methods of preparation of various brews brought to light some surprising facts. In a series of investigations in the Transkei it was found that the beers were commonly brewed in large drums containing asphalt and fuel oil residues. Such containers are sometimes fitted with condensation tubes improvised from car exhausts, bicycle frames and petrol pump hose. Furthermore, the basic brew may have stimulating additives such as carbide, bhang and metal polish. Small wonder that the research workers thought they were on to a promising supply of polycyclic hydrocarbons and other potential carcinogens. However, as the work has been extended and has included other areas in which the tumour is common, these early suspicions seem less likely. In some of the areas of high incidence in West

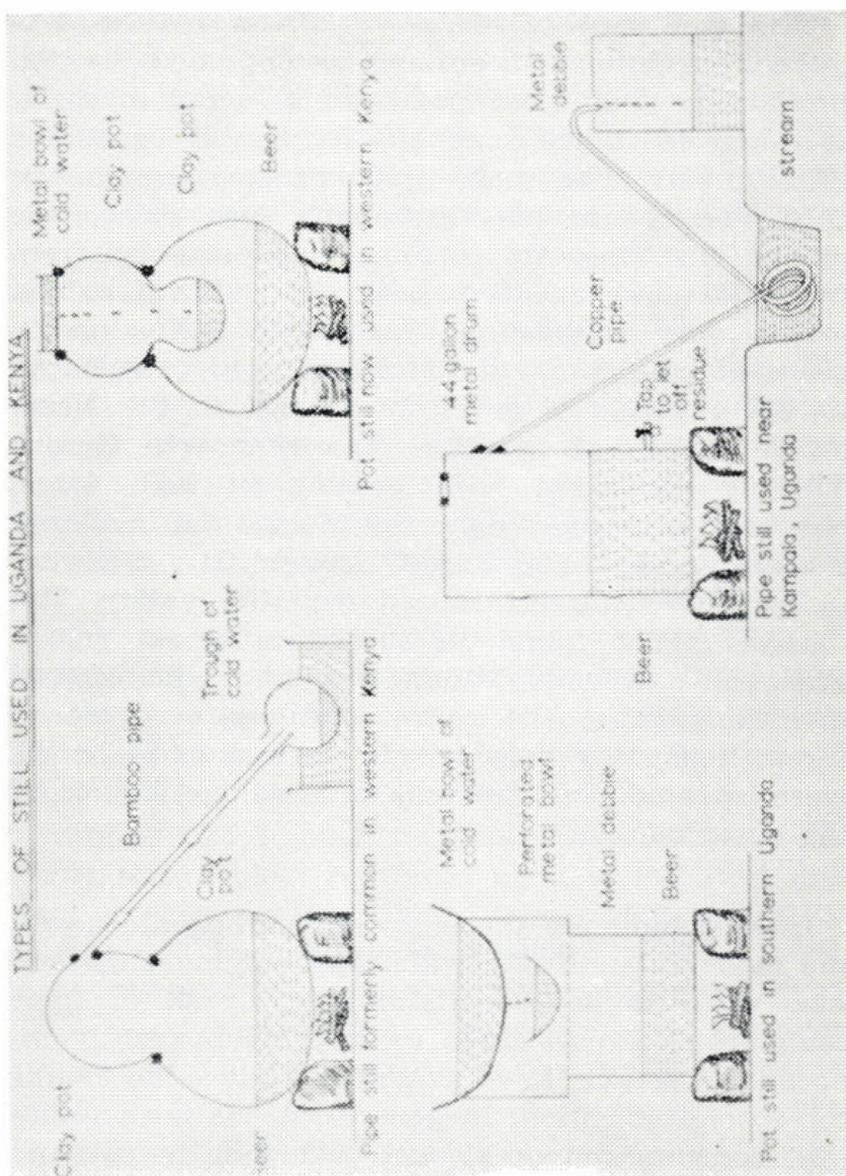


Fig. 3. A variety of beer stills.

Kenya (Fig. 3), traditional earthenware pots with bamboo pipes are still in use and there is little evidence that additives are relevant. A similar anticlimax has followed the identification of nitrosamines in spirits in Zambia. The nitrosamines are a group of carcinogenic substances and are the only carcinogens known to produce carcinoma of the oesophagus in experimental animals. However, no evidence of nitrosamines has been found in the brews of West Kenya. Identification of these substances involves sophisticated chemical techniques, and it is probable that further investigations are required.

Recently, we have been associated in a small way with an investigation of locally brewed beers carried out under the auspices of the British Medical Research Council. A Cambridge medical student spent some weeks in 1969 enquiring into methods of brewing and drinking habits. He

in many parts it makes up more than 50% of the crops. In Uganda, however, where cancer of the oesophagus is rare, the growing of maize has been discouraged by the Government in the belief that it encourages soil erosion, and it takes up less than 5% of the food acreage. While this may take us only a little nearer an understanding of the carcinogenesis of the tumour, it may provide the explanation of the strange limitation of the disease by national boundaries; this is surely more consistent with a chemical factor than with any conceivable infective agent.

CARCINOMA OF THE LIVER

When we come to the third neoplasm I have chosen, carcinoma of the liver or hepatoma, we find evidence implicating both chemical and viral agents. This is a malignant tumour which, though of world-wide distribution, is very much more common in some parts than in others. It is one of the common cancers of Africa, and attains an astonishingly high incidence in Mozambique where it is said to produce 98 cases per 100,000 of the population per year; the comparable figure for Europe and America would be between 1 and 5 per 100,000.

It is a malignant tumour which, because it arises in a large solid organ, produces few symptoms until it is of large size. We see it commonly in Kenya, and, because of its late presentation, there has been little one could offer in the way of therapy. A recent discovery offers hope that this gloomy picture may change; a protein (the alpha-fetoprotein) has been found specifically in the sera of hepatoma patients and this offers the hope of early diagnosis, leading to early surgery.

Different forms of liver disease are common in many tropical countries. Apart from carcinoma of the liver, two which are common in Africa and are relevant to this discussion are:

- (1) Acute hepatitis — a viral disease characterised by degenerative changes in liver cells; it is usually self-limiting and most cases are followed by complete recovery.
- (2) Cirrhosis of the liver. In this there is widespread scarring of the liver, which is nodular due to regeneration of liver cells following on previous damage. It should be noted that regeneration entails active multiplication of liver cells.

Recently it has been suggested that these diseases may be inter-related, but the evidence is fragmentary and inconclusive. There is however evidence that viral hepatitis in the tropics is a more serious disease than that seen in temperate climates; in Nairobi, Dr. Bagshawe and her colleagues have shown that it is associated with a high morbidity and high mortality.

Recent work suggests that this may be associated with the presence in the blood of a virus-like particle known as the Australia antigen; this usually disappears rapidly as patients recover from hepatitis, but in a small proportion it persists, and we have found it in a considerable number of patients suffering from cirrhosis and hepatoma. Until recently it was believed that hepatitis rarely produced permanent scarring or cirrhosis of the liver, but this was based on work in temperate climates and it seems likely that the more virulent hepatitis of the tropics may result in cirrhosis (Fig. 5). Hepatoma may arise in an

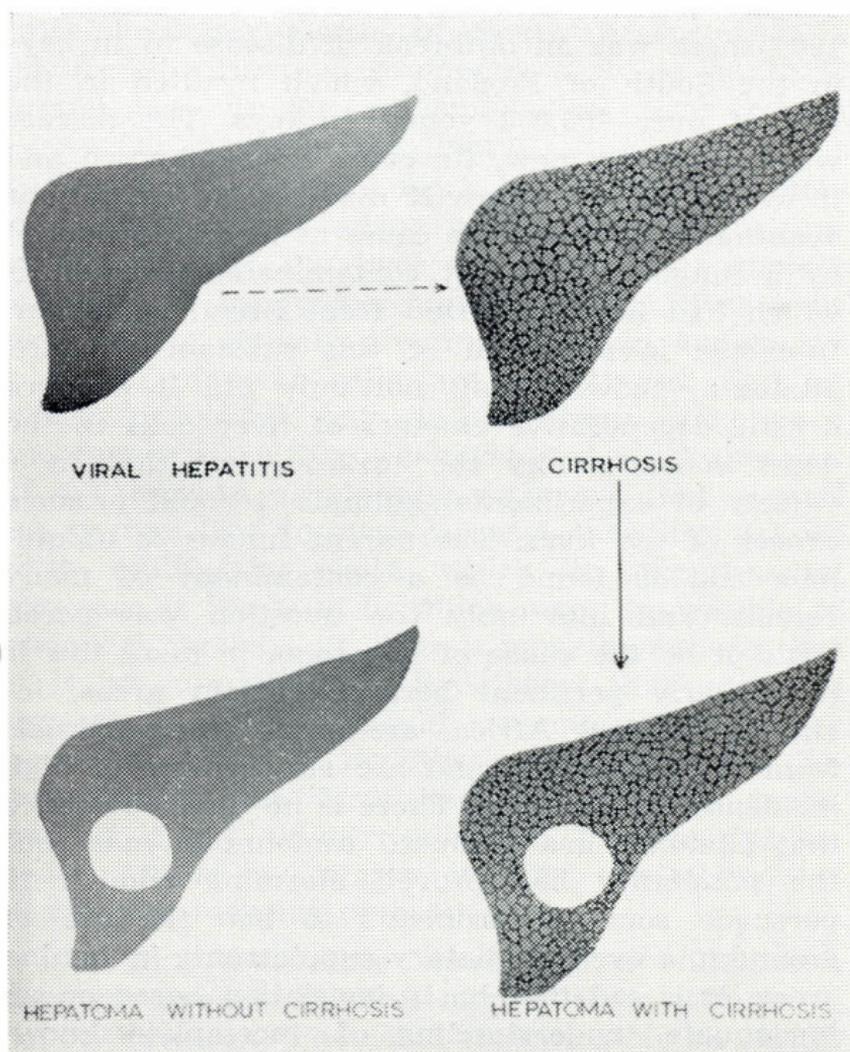


Fig. 5. Hepatitis may lead to cirrhosis. Hepatoma occurs commonly in cirrhosis. Hepatoma occurs less frequently in non-cirrhotic livers.

otherwise normal liver but it is particularly liable to do so in a cirrhotic liver. In Europe and America, about 10% of cirrhotic livers are found at post-mortem to have developed hepatomas; in Africa the figure may be as much as 50%. We are a long way from implicating a virus as a cause of liver cancer; the most we can say at present is that in countries like Kenya we have three common forms of liver disease — hepatitis, cirrhosis and hepatoma. The first is a viral disease, and a virus-like particle found in it may on occasions also be demonstrated in the sera of patients with the other two diseases, and there is some pathological evidence of transition from hepatitis to cirrhosis, and of cirrhosis to hepatoma.

In the experimental investigation of possible cancer-producing chemicals, the liver has been extensively used as a target, but a sudden interest in the possibility of this being relevant to human disease came from an improbable association of turkey farms in the South of England and mouldy peanuts from Brazil. In the summer of 1960 there was an outbreak of disease in turkeys in the South of England, which resulted in the loss of over 100,000 young turkeys. The disease was apparently new, its cause was unknown and it was labelled "turkey-X disease". Investigations eventually identified the cause as a toxin produced by a fungus which had contaminated groundnuts which had been imported from Brazil as fodder. Intensive investigation of this substance, named aflatoxin, showed that, not only did it produce drastic degenerative changes of liver cells in the doses consumed by the turkeys, but that in a variety of experimental animals it could produce cancer of the liver. The parent fungus is ubiquitous and is found as a contaminant of many cereals, and inevitably the question was posed could it be the cause of hepatoma in man; this is particularly pertinent because certain areas, including tropical Africa, are areas where cereals form the staple diet and are also centres of high incidence of hepatoma. There is no direct evidence that aflatoxin has produced tumours in man, but the possibility has proved alarming enough to persuade some governments to ban the use of groundnuts even as dietary supplements in famine areas. It is sad that hasty legislation based on an inadequate understanding of incomplete knowledge should lead to the condemning of desperately needed food supplies; it is likely that more

children have died as a result of this deprivation than could have contracted hepatoma from its possible carcinogenic potential. It is too easy in these days of rapid dissemination of half-truths, for panic reaction to follow the publication of such findings. One must, therefore, emphasise that the evidence that aflatoxin may be a factor in human disease is purely circumstantial. Clearly, however, it must be investigated. In Kenya this is being carried out by Dr. Linsell of the International Agency for Research on Cancer. He has examined samples of food, cooked and ready for eating, and has found that it frequently contains aflatoxin; his work shows that there is an association between the quantities of aflatoxin ingested and the current frequency of liver cancer. In Swaziland, it has been shown that in the areas of higher relative incidence of hepatoma, the opportunities of ingesting aflatoxin are greater. Once again we find ourselves beset with the dangers of drawing hasty conclusions from inadequate data. However, many workers would agree with Professor Oettlé of South Africa, that a naturally occurring carcinogen such as aflatoxin would best fit the epidemiological facts known about carcinoma of the liver.

Recent experimental work has shown that some of the compounds which have been used to produce cancer of the liver are much more rapidly effective in producing tumours if the liver cells are already actively dividing. Division and multiplication of liver cells are an integral part of cirrhosis, and it may be that here we have a meeting point of the chemical and viral theories. If one accepts, as already suggested, that a viral agent may lead to cirrhosis, one then has a liver with multiplying cells, which on experimental evidence is likely to be much more susceptible to chemical carcinogens. This is mere hypothesis, but it is by forming fresh hypotheses that advances are made, and we should remember that it has been stated that "a hypothesis which becomes dispossessed by new facts dies an honourable death, and, if it has already called up for examination those truths by which it was annihilated, it deserves a moment of gratitude".

It is not long since there was a widespread fatalism amongst medical men in their attitude to cancer research. The viral theory, after an initial period of euphoria, had turned up some interesting animal tumours with rather remote resemblance

to human tumours. The chemical school on the other hand had become an introverted minority, who, to the clinically-minded physician seemed more concerned to establish a satisfactory animal "model" than to relate it to human disease. This defeatist attitude is fast disappearing and it is no longer surprising to find eminent authorities suggesting that three-quarters of our cancers have their origins in the environment. We have learnt how to control the environment in preventing the spread of bacterial infections and parasitic diseases — the fact that we do so inadequately is a matter more for the politicians than the doctors. In cancer, the road ahead is to identify the environmental agents, so that eventually we may learn to control them. A surgeon of the fourteenth century, Guy de Chauliac, wrote in a prologue to his textbook "we are like children standing on the shoulders of a giant, for we can see all that the giant can see and a little more".

The giant has grown since those early days, and perhaps we may not immodestly claim that the child too has grown, and one has the exciting feeling that we may now at last be on the threshold of discoveries which may lead to the control of this formidable group of diseases.

ACKNOWLEDGEMENTS

I am indebted to Dr. C. A. Linsell and Miss Paula Cook for permission to quote from their work on aflatoxin and oesophageal cancer.