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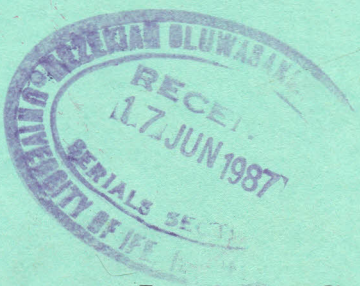
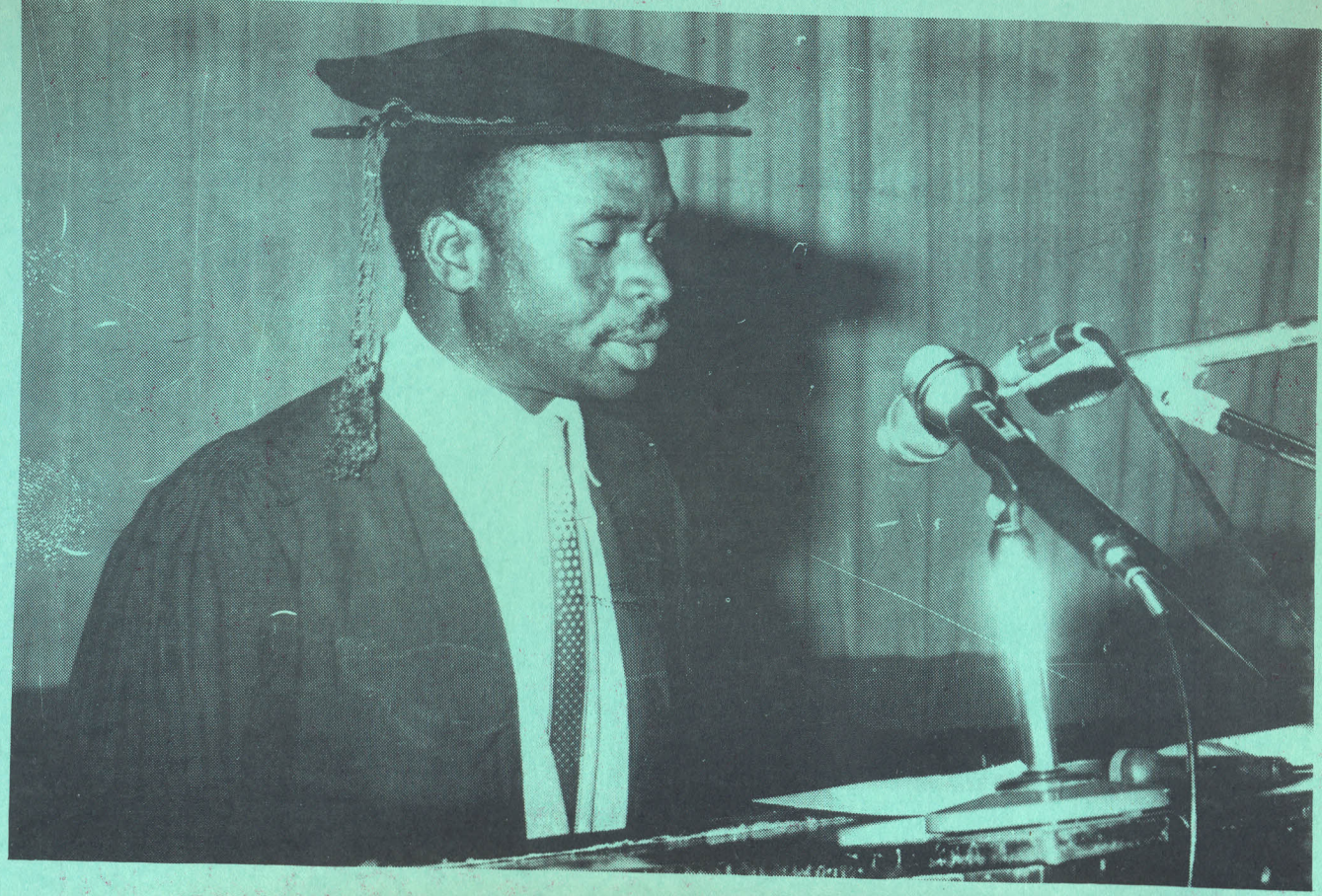


Inaugural Lecture Series 65

CANCER IN OUR SOCIETY

by S. O. OLUSI

UNIVERSITY OF IFE PRESS



Professor **S. O. OLUSI**

CANCER IN OUR SOCIETY

by

S. O. OLUSI
Professor of Chemical Pathology

An Inaugural Lecture Delivered at the University of Ife on Tuesday, 15th November, 1983.

Inaugural Lecture Series 65

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I. INTRODUCTION AND DEFINITIONS

The word 'Cancer' has different meanings. In astronomy, it is a constellation of the zodiac lying between Leo and Gemini at about 8 hours 25 minutes right ascension, and 20° north declination. It contains the well-known star cluster called Preesepe or the Beehive. In astrology, Cancer is the fourth sign of the zodiac considered as governing the period between June 22nd and July 22nd. Its representation as a crab (or lobster or crayfish) is related to the crab in Greek mythology that pinched Heracles while he was fighting the Lernaean hydra. Crushed by Heracles, the crab was rewarded by Heracles' enemy, Hera, by being placed in the heavens. In religion, the word connotes a moral disease that leaves the soul completely disintegrated and prevents its entry into Heaven.

In medicine, Cancer is any one group of over 100 related diseases characterised by the disorderly and uncontrolled multiplication of abnormal cells in the tissues of the body. Such cells no longer respond to the external or their own internal or subcellular controls that restrain them and keep them in balance with all other cells in the body. Instead of dividing and forming more of themselves in a restrained and totally organised way or simply staying where they are and doing what they should do, making proteins, carrying haemoglobin, fighting infections or transporting fats, cancerous cells take off on their own, displacing and destroying other cells until the patient dies. Conceptually therefore, a cancer cell may be likened to a wayward, over-ambitious, nihilistic and egocentric non-conformist who in his ambition to displace and destroy his colleagues digs the foundations of his house,

forgetting that when his house collapses it will collapse not only on the heads of those he is seeking to destroy but also on his own head.

In the beginning inaugural lectures were like sermons and were I to conform with original tradition, I might choose for example to speak on any of the stated definitions of cancer, be it astronomy, astrology or religion. But times and traditions have changed and inaugural lectures are now confined to one's discipline. I have therefore decided to confine myself to the medical aspect of cancer. Inaugural lectures, unlike lectures delivered before a Science Academy, are meant for a large and heterogenous audience and are therefore not supposed to be too academic. I will therefore endeavour to tell you as simply as possible what is known about all aspects of cancer. In doing so, I of course will draw copiously from my personal research data.

II. HISTORY OF CANCER

Cancer, like other diseases is much older than man himself, as Professor Roy Moodie[1] has proved by his discovery in Wyoming of a dinosaur with a bony tumour in the caudal vertebrae. The age of such a specimen must be measured in millions of years Cancer is mentioned in the Papyrus Ebers (1500 B.C.) and in the oldest remants of the literature of India and Persia Herodotus mentions that Democedes in 520 B.C. cured Atossa, the daughter of Darius Hystaspis, of breast cancer, and Hippocrates burnt out a carcinoma of the neck, the earliest record of diathermia. Paracelsus gave classic descriptions of cancer well before the end of the sixteeth century. Livers turning malignant, lungs and stomachs eaten away by cancer have always been a horrifying part of medicine; they have been with us from the beginning, yet until a few years ago no one knew

what they were, where they came from or how they killed us.

Much of the confusion of what was and was not cancer came about because for centuries cancers were confused with other diseases. Looked at superficially even today, leprosy can easily be mistaken for the slowly eroding squamous cell carcinomas of the face and hands, echinococcal cysts for hepatomas of the liver, tuberculosis for lung cancer. It was only when the microscope began to be used and precise microscopic evaluation of diseased organs and pathologic tissues became possible that the confusion about what was and what was not cancer finally began to be cleared up.

By the end of the nineteenth century, pathologists were able, by looking at diseased tissues under the microscope, to identify any number of malignancies by the type of cells that made them up, malignant melanomas, rhabdomyosarcomas, astrocytomas, adenocarcinomas, hepatomas. But the names meant nothing. Patients died just as slowly and just as horribly with a correct diagnosis as those who had died misdiagnosed or with no diagnosis at all. The ability to recognise the various cancers was only the beginning. Today, we not only can diagnose cancer, we can prognosticate on its outcome depending on the tissue involved, and in a few cases we can provide paliative or definitive treatment.

III. SOME STATISTICS

What is the extent of the cancer problem in human societies? In the United States of America, cancer is the second major killer, being responsible in recent years for about 300,000 deaths per year[2]. It is estimated that about one million people in the United States receive treatment for some kind of cancer each year. Of these,

more than half are new cases, having been diagnosed for the first time during the year. If present trends continue, about one fourth of the nation's citizens will sooner or later develop cancer. The commonest cancer in the male in the United States is lung cancer, followed by those of the prostate, colon and rectum, in that order.[3] In the female, the commonest cancer is that of the breast, followed by those of the colon and rectum and the uterus.

In European countries, the commonest cancers are those of the lung, prostate, breast and blood forming elements. For example, mortality due to cancer of the lung has risen in 24 European countries during the 20-year period from 1955 to 1974. In 1974, the mortality rate for lung cancer was 154.5 per 100,000 persons in Scotland; in England and Wales 134.8; in the Netherlands 127.1; in Belgium 120.5; in Portugal 40.8; in Norway 48.8; Sweden 56.5; and Spain 60.8. For prostate cancer in men. Sweden with 38.9 per 100,000 men had the highest rate; Switzerland 35.3; Norway 30.7; Hungary 29.2; Belgium 28.1; the Federal Republic of Germany 27.4; and France 27.0. The lowest rates were those for Bulgaria 10.3, Greece 11.5, Yugoslavia 13.2, Poland 13.8, Romania 14.5; Italy 18.8 and Czechoslovakia 19.5. For breast cancer in women in 1974, the Netherlands with 37.8 per 100,000 women had the highest rate followed by England and Wales 36.5, Ireland 35.8, Denmark 35.6, Scotland 34.8, Switzerland 33.0 and Belgium 31.0.

In Nigeria, cancer statistics, like any other statistics, may be rather nebulous. Just as there are no accurate statistical data on our population figure, there is very little or accurate information on the incidence of cancer in the Nigerian society. However, we know that cancer ranks behind the major causes of death: malnutrition, malaria, infections and infestations and accidents.

Table 1

Cancer Incidence by Site at Ife University Teaching Hospitals Complex (1978-1982)

Site	*Number of Cases*	*Percentage*
All sites	612	100.00
Lymphomas and Leukaemias	115	18.79
Breast	105	17.15
Gastrointestinal Tract	96	15.69
Cervix	83	13.56
Liver	78	12.75
Skin	36	5.88
Uterus	23	3.76
Others	72	11.76

Table 2

Cancer Incidence by Sex and Age at Ife University Teaching Hospitals Complex (1978-1982)

	Number of Cases	*Percentage*
Total	612	100.00
Females	338	55.23
Males	274	44.77
Adults	544	88.89
Children	68	11.11

In a study we conducted on the incidence of cancer at the Ife University Teaching Hospitals Complex (see Table 1), we found that there were 612 histologically proven cases of cancer between 1978 and 1982. Of these, 544 (88.89%) were adults and 68 (11.11%) were children. Also there were 338 (55.23%) females and 274 (44.77%) males (Table 2). It will thus appear that the incidence of cancer among the female population in Nigeria is higher than that of the male. So, in our society, the female, already a poor victim of domestic problems and societal inequalities, is now being further threatened by the big monster that is cancer. Why is the incidence of cancer in females higher than in males? A look at Table 1 will show that the commonest cancers in our society are those of blood cells, breast, gatrointestinal tract, cervix and liver in that order. Cancer of the breast, cervix and uterus alone account for 34.47% of all cancers in our society. In females the commonest cancer is that of the breast (Fig. 1) while in males the commonest cancer is that of the liver. However, compared to other countries, breast cancer is infrequent in Nigeria. In children, the commonest cancer is Burkitt's lymphoma.

Edington and Maclean[4] reported a total of 648 cancers in Ibadan between 1960-1963. 318 were males while 330 were females. From available data, Maclean calculated the resultant annual age-specific incidence per 100,000 population of all types of malignant disease diagnosed in the Ibadan population (Table 3). Examination of the Table shows that the age specific incidence for males in Nigeria correspond fairly closely, from age 15-45, with those of the U.S., whites and non-whites. In the younger age group, the overall cancer incidence in Ibadan was higher than in the United States due to the great prominence of Burkitt tumour which attains the astonishingly high incidence of

Fig 1 – A female with cancer of the breast.

Table 3

The Annual Age specific incidence per 100,000 Population of Malignant Disease (all types) in Ibadan.

Age Group	*Estimated Ibadan Population*		*Total Malignancies (3 Years)*		*Annual Age Specific Incidence Per 100,000*	
0 – 4	M	F	M	F	M	F
0 – 4	40,000	40,000	14	5	11.66	4.16
5 – 9	29,000	34,000	25	14	28.73	13.72
10 – 14	24,000	23,000	19	8	26.41	11.59
15 – 19	22,000	15,000	11	6	16.66	15.55
20 – 29	45,000	52,000	36	34	26.66	21.15
30 – 39	27,000	33,000	47	55	58.02	56.56
40 – 49	14,000	17,000	64	81	152.38	158.82
50 – 59	8,000	7,000	41	86	170.83	409.52
60 – 69	4,000	3,000	48	30	400.00	333.00
70 +	1,000	1,000	5	3	166.00	100.00
Age N.K.	23,000	15,000	8	8	11.59	17.7
All ages	23,000	15,000	318	330	45.00	45.5

Source: Edington and Maclean, 1965.

21.8 per 100,000 among Ibadan boys aged between 5-9 years. After the age of 45, the Ibadan male figures fall away from those of the United States until after the age of 69 when there is a drop in cancer incidence. This apparent drop can be attributed to the fact that fewer Nigerians than Americans live for more than 69 years. Another interesting deduction that can be made from Table 3 is that the annual age specific incidence per 100,000 in females (646.05) is higher than in males (407.89) aged between 20 and 59 years. This confirms our finding from Ife that the incidence of cancer is higher in females than in males. It ought to be pointed out that the above figures were derived from hospital diagnoses and for every case that comes to the hospital in Nigeria, there will be many more that will refuse to come.

In 1981, Professor Abioye[5] reviewed data obtained from the Ibadan Cancer Registry between 1960 and 1980. In this twenty-year period, a total number of 17,496 cancers, made up of 9,091 females and 8,405 males were recorded. The most commonly found malignancies in Ibadan are carcinoma of the cervix, malignant lymphoma, primary liver cell carcinoma, carcinoma of the breast and Burkitt's lymphoma. A comparison of the Nigerian data with those of developed countries show that cancer of the lung, colo-rectal and uterine body which are major killers in the Western countries are relatively rare in Nigeria and other tropical African countries. On the other hand, cancer of the liver, cervix, uteri and chorio-carcinoma have higher frequencies in the tropics than in Europe or North America.

IV. CAUSES OF CANCER

Although the exact mechanism of how cancer starts remains a mystery, it has been possible to identify many

actual and potential causes of cancer. There is little doubt that prevention is currently our most effective weapon against cancer. If human exposure to known cancer-causing agents could be avoided and if other factors involved in stimulating cancer could be modified, the cancer problem would be reduced to a fraction of its current size. For convenience, cancer can be divided into those of defined origin, those for which aetiological hypotheses can only be deduced and those of unknown aetiology.

Group 1. Cancers Caused by Defined Exogenous Factors

These are predominantly tumours in adults, arising in the skin, respiratory tract, upper digestive tract, liver, pancreas and bladder. It also includes some other tumours of the endometrium and blood-forming organs. Personal habits, notably cigarette smoking, alcoholic beverage consumption and sunbathing are by far the most important stimuli identified, causing from 25% to 50% of all cancers in males in different populations. All studies increasingly emphasize the overwhelming role of cigarette smoking in human cancer not only *per se*[6] but also as enhancing the effects of other agents e.g. alcohol or kolanut chewing. While less adequately documented, primary liver cancer in Africa and Asia is believed to arise in hepatitis B virus carriers exposed to aflatoxin. Studies on the association between Epstein-Barr virus and Burkitt's lymphoma in Africa, and nasopharyngeal cancer in China suggest that other exogenous factors may play a modulating role.

Group II. Cancers of Probable Environmental Origin

This group is made up predominantly of tumors of the gastrointestinal tract, stomach, large intestine, endocrine related organs (prostate, ovary, breast, uterus cervix) and

some tumours of the genito-urinary system. This group forms approximately 40% of cancers in males and 60% to 70% in female.[8]

Group III. Cancer of Unknown Aetiology

For a number of tumours in children, bone and soft tissues and blood system, only a few discrete causal factors have been determined and the majority have known causes. Causes of cancer may therefore be summarised as in Table 4 below.

Table 4

CAUSES OF CANCER

1. **Cultural Habits**
   - i. Cigarettes
   - ii. Alcohol
   - iii. Betel liquid
   - iv. Sunlight

2. **Biological Agents (Viruses)**
   - i. Liver cancer – aflatoxin and hepatitis B
   - ii. Burkit's lymphoma -- EB virus
   - iii. Nasopharyngeal carcinoma -- EB virus

3. **Impaired Immunological Surveillance**

4. **Chemicals and Environmental Pollution**
   - 19 definite hazards
   - 18 probable hazards

5. **Ionizing Radiation**

My Own Hypothesis of Carcinogenesis in Nigeria

As a House Officer at the University College Hospital, Ibadan, in 1973, I was surprised to see that most of the children that presented with cancer were malnourished and were generally from the poor socio-economic groupings. When I went to Manchester for my postgraduate studies in 1974, I decided to look at the host responses in malnutrition.

Based on my studies on kwashiorkor, marasmic kwashiorkor and obesity (see Fig 2), I formulated a working hypothesis for a causation of some cancers in Nigeria. Simply, the hypothesis (Fig. 3) is that poverty leads to malnutrition which in turn leads to impairment of immunological responses and depression of immunological surveillance. A person with a depressed immunological surveillance in the presence of favourable modullating factors will develop cancer.

Perhaps one of the best scientific approaches to test the validity or otherwise of this hypothesis is to carry out longitudinal and prospective studies on children with malnutrition to find out the incidence of cancer amongst them later on in life. This has been my primary research interest since 1977 and were I to give this inaugural lecture in 1987, I probably would have been in a position to give you some insight into my findings. But it will appear that time is against me. I propose to let you know instead some of the associations we have found between poverty, immunity, carcinogens, heredity and cancer.

a. Socio-economic Status of Cancer Patients in our Society

A scoring system based on the level of education, occupation, income, type of accommodation and family size was used to classify 200 randomnly selected cancer pati-

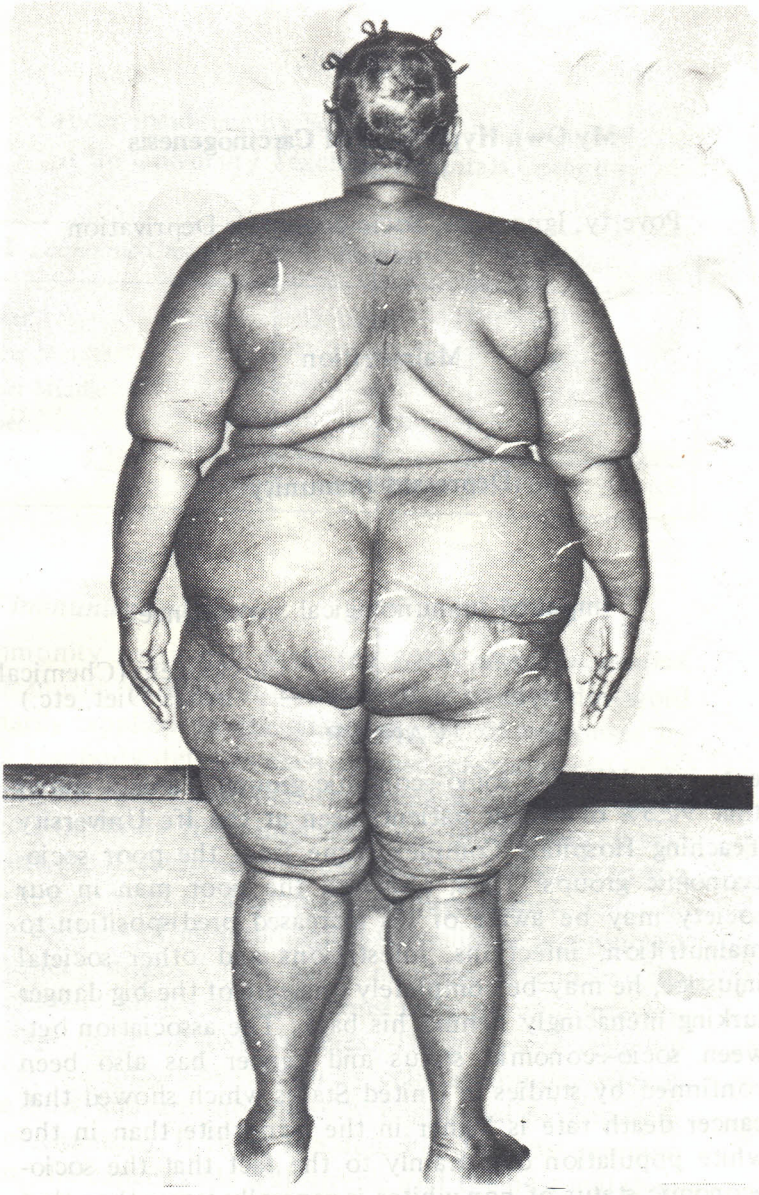
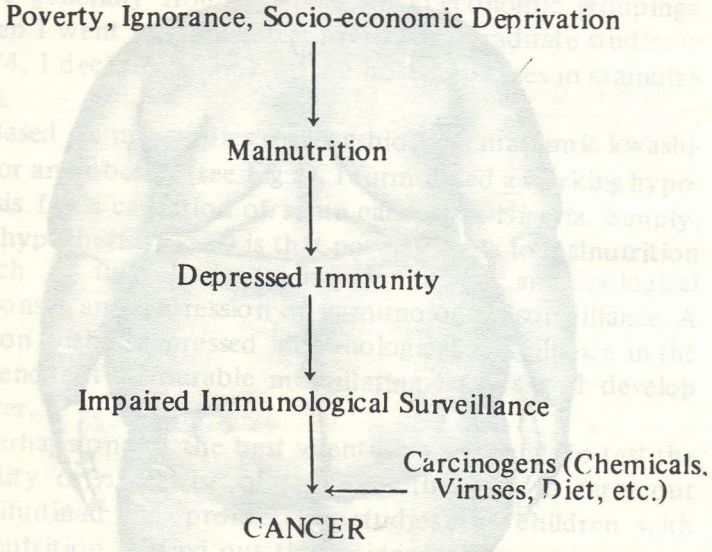


Fig 2 – A female with obesity

Fig 3

My Own Hypothesis of Carcinogenesis



ents into different socio-economic groups. Table 5 shows that 92.5% of cancer patients seen at the Ife University Teaching Hospitals Complex come from the poor socio-economic groups. Thus, although the poor man in our society may be aware of his increased predisposition to malnutrition, infections, infestations and other societal injustice, he may be completely unaware of the big danger lurking menacingly behind his back. The association between socio-economic status and cancer has also been confirmed by studies in United States which showed that cancer death rate is higher in the non-white than in the white population due mainly to the fact that the socio-economic status of non-whites is generally lower than that of whites.

Table 5

Cancer Incidence by Socio-Economic Grouping at Ife University Teaching Hospitals Complex

Socio-Economic Group	*Number*	*Percentage*
Lower	136	68
Lower Middle	49	24.5
Upper Middle	15	7.5
Upper	–	–
	200	100

b. Immunity and Cancer

Immunity originated from the Latin word *immunitas*, which means 'exempt from taxes'. It is an everyday word ordinarily applied to the elaborate set of responses by which the body defends itself against infections and infestations. We now know that the immune system not only protects the body from infections and infestations, it also prevents the development of cancer. This brings us to the important concept of immunological surveillance.

The concept of immunological surveillance as proposed by Burnet[9] suggests that small numbers of cancer cells with altered surface antigens constantly develop in every individual as the individual ages. These cancer cells are however recognised as foreign by cellular immune system of the host and are subsequently eliminated by immunologic mechanisms. If there is a defect in the host immune system, the cancer cells will survive and the host will then develop cancer.

A very convincing evidence for an association between oncogenesis and immunity is the fact that the frequency of malignancy in patients with primary immunodeficiencies is roughly 10,000 times greater than that of the general age-matched control population. Almost everyone of the primary immunologic abnormalities is associated with distinctive constellations of malignancy which although there is much overlaping, give support to speculations concerning oncogemic mechanism.

Patients with infantile x-linked agammaglobulinaemia (Bruton-type) lack humoral immunity. They do not make antibodies in response to antigenic stimulation. Isohaemaggalutin titers are absent and immunoglobulin levels are extremely low. On the other hand, these children reject skin grafts and manifest delayed hypersentivity skin reactions in normal fashion. This implies that cell-mediated immunity is intact. Studies on these patients have shown a high rate of cancer. Patients suffering from severe combined immunodeficiency formerly called lymphopenic agammaglobulinaemia lack both humoral and cell-medicated forms of immunity. In spite of the rarity of this disease and the early deaths from infections, 3 reports of associated malignancies have appeared in the literature.

In children with Wiskott-Adrich disease, IgM levels are very low, IgG levels are usually normal and IgA may be normal or high. Cell-medicated immunity is intact early in the disease, but with time these children become anergic to DTH skin tests. Such patients meet early death either from overwhelming infection, massive bleeding secondary to thrombocytopenia or cancer. Roughly, one out of ten die of cancer which is usually of the lymphoreticular type.

Chronic antigenic stimulation followed by frank malignancy is also seen in certain patients with the 'common variable' form of immunodeficiency formerly called late-onset acquired sporadic hypo–or dysgammaglobulinaemia.

A significant number of these patients later develop carcinomas of the stomach or rectum, benign follicular lymphoma and Hodgkin's disease.

Of further interest is the observation that deficiency of IgA has been associated with cancer of the stomach. Ataxia-telangiectasia is a neurologic disease of childhood which begins with ataxia sometimes as early as 6 months of age; telangiectasias over the ears and eyes often becomes apparent several years thereafter. Immunologically, these children usually have low IgA level and inadequate cell-medicated immunity. The incidence of cancer in these children is remarkably high; at least 10% die of cancer.

In a study of some immunological parameters in cancer patients here at Ife (Table 6), we found that the percentages of T and B lymphocytes were significantly lower in cancer patients than in age-matched controls. Similarly, IgA and IgM concentrations were significantly lower in cancer patients than in the control. What is more, one case of cancer of the stomach associated with IgA deficiency was discovered. These studies show that there is an association between immunodeficiency and carcinogenesis.

c. *Carcinogens and Cancer*

Carcinogens are agents that induce cancer formation in cells or tissues. Such agents may be chemicals or viruses. They may be in our diet, or in the water we drink or in the air we breathe or in our work-place, or in the cosmetic agents that we use.

Table 6

Some Immunological and Biochemical Indices in Normal Nigerians Compared with those with Cancer

	Controls	*Cancer Patients*	*P Value*
% E rosettes	65 ± 1.34	36 ± 6.16	P < 0.01
% B rosettes	26 ± 0.91	15 ± 6.5	P < 0.01
IgA (mg/100ml)	235.40 ±	209.14 ± 1924	N. S.
IgM (mg/100ml)	244.70 ± 41.69	152.55 ± 14.33	P < 0.05
IgG (mg/100ml)	3,044.0 ± 139.55	1,923.60 ± 147.36	P < 0.01
Albumin (g/100ml)	3.14 ± 0.10	2.38 ± 0.06	P < 0.01
Transferrin (mg/100ml)	240.6 ± 38.9	118 ± 13.6	P < 0.01
Cmplement C3 (mg/100ml)	120.8 ± 18.3	79.6 ± 20.3	P < 0.01

Carcinogens in our Diet

A variety of dietary factors have been associated with cancer causation, although in some cases their role in human cancers is still uncertain. One of the most widely discussed of these agents is a combustion product called benzo -a- pyrene, a member of a class of compounds called polycyclic hydro-carbons, many of which readily cause cancer in animals. Benzo-a-pyrene is found in smoked foods, bread, roasted coffee, and steaks and other foods broiled over charcoal like roasted maize or roasted plantain. Its very high level in home-smoked foods has been suggested as the cause of the extremely high incidence of stomach cancer in Iceland, where home smoking is very popular. The relatively high incidence of stomach cancer in Nigeria may also be associated with the high consumption of roasted maize, plantain, yam and suya.

Compounds known as nitrosamines are also potent carcinogens in animals. Nitrosamines can be formed in the digestive tract when a common food preservative, nitrite, combines with amines that result from the digestion of proteins. Nitrates, also commonly used to preserve foods like sausages, bacon and vegetable salads, can be changed into nitrites in the body and may cause cancer.

The cancer-causing potential of caffeine, the stimulant found in coffee and tea and to a lesser extent in cola and cocoa, has been hotly debated. In a number of tests, caffeine has been shown to enhance the effects of certain known cancer-causing agents, including some tumour viruses. On the other hand caffeine seems to protect against the effects of other cancer-causing agents. Another constituent of coffee, chlorogenic acid, has been shown to speed the formation of nitrosamines. If this reaction occurs in the stomach, the common breakfast combination of coffee and bacon or sausages which are preserved with

nitrates and nitrites, may lead to significant exposure to one of the most powerful cancer-causing agents known.

Other dietary risk factors which show positive correlations in high risk populations include the high consumption of dried salted fish, smoked fish and fat (which has been associated with cancer of the breast). Here at Ife, we have found an association between a long history of kola-nut chewing and cancer of the rectum, an association that requires further investigation.

Cancer in Water and Air

As the story of Duluth and Lake Superior so clearly demonstrates, even the purest water can contain hidden hazards that may contribute to the development of cancer. Chlorination, the very process that is supposed to purify water may lead to the formation of certain carcinogenic substances such as chloroform, carbon tetrachloride and tetrachloroethylene.

Air pollution also contributes to the human cancer problem, although in most cases the carcinogenic culprits in the air have not been identified. Zinc, lead and copper have, however been incriminated. For a wide variety of cancers including cancer of the lungs, the incidence is higher among people living in urban areas than residents of rural communities.

Cancer and Habits

In Travancore on the southwestern coast of India, people are in the habit of chewing a mixture of betel nuts, tobacco and lime from crushed sea shells. Seventy-five per cent of the oral cancers in that regions are attributed to the effects of this habit. Oral cancer also afflicts people in the southeastern United States who dip snuff and those in South Asia who practise a habit called chutta-smoking –

placing cigars with the lighted end in the mouth. Clay pipe smokers of Ireland are prone to cancer of the lip. In Kashmir, the natives used to bind small charcoal-burning earthen ovens around their waists for warmth during the cold season. Many developed cancers of the abdominal wall as a result.

Probably the most dramatic example of the cancer-causing effects of a particular custom is the phenomenon of cigarette-smoking. In the United States about 30 percent of the cancer deaths in men are directly attributable to the carcinogenic effects of cigarette smoking and at least 75 percent of lung cancer cases would not occur if the victims had not smoked. Although at the moment the incidence of lung cancer is low in Nigeria compared with other developed countries a study of the smoking habits of Nigerians, particularly the elites and university students, seems to indicate that cancer of the lung will be a major killer in this country during the next century. In addition to cancer of the lung, cigarette smokers also face increased risks of dying of cancer of the larynx, oral cavity, oesophagus, bladder, kidney, stomach, prostate and pancreas.

The risk of developing smoking-caused cancer is directly related to the extent of exposure to the carcinogenic agents in cigarette smoke. Thus the risk increases the longer one smokes and the greater the number of cigarettes smoked daily. Risk is also effected by the extent of inhalation and the amount of tars present in the smoke. The use of low-tar filtered cigarettes is associated with a lower cancer risk, although it is still substantially higher than that of non-smokers. Heavy pipe and cigar smokers are also more likely than non-smokers to develop cancer of the lung and cancer of the kidney, but their risk is only about half as high as that of cigarette smokers, probably because few pipe and cigar smokers inhale.

Extensive studies have been done to identify the cancer-inducing agents in cigarette smoke. More than 1,200 components have been identified in tobacco smoke, 95 percent of them in the "tar" or smoke condensate. Many of these components are known carcinogens, cocarcinogens and tumour promoters. Included are benzo-a-pyrene, the major carcinogen in coal tar, chrysene and methychrysenes, terpenes, catechol and the radioactive element polonium 210.

Some of you may ask: If cigarette smoking causes cancer, why is it that some people who have been chain smoking for more than 30 years are still alive and well? People vary in their sensivity and genetic constitution. It is the same with power, education and wine. Some people get intoxicated and become destructive with little quantities while others take large quantities but remain sober and constructive.

Carcinogens in our Environment

Although there are many carcinogens in our environment, I have in the past four years directed my attention to those associated with the petroleum industry. Crude petroleum is a mixture of aliphatic, naphthene hydrocarbons. The olefine or unsaturated type is produced by cracking of crude oil. Chemicals derived from crude oil include kerosine, bitumens lubricating oils, benzene, toluene, 3,-4-benzepyrene gases containing high proportions of olefines like propylene, butylene, tars, asphalt, pitch and gaseous emissions like sulphur and its oxides, carbon monoxide and oxides of nitrogen. Most of these chemicals cause cancers after long exposure and the latent period varies from ten to twenty five years.

In 1974, the American Petroleum Institute published the results of a survey of death among petroleum refinery worker.[10] The study selected workers in 17 of the nation's

251 refineries to provide a representative sample according to location, ownership and size. The mortality study involved 20,163 workers with a total of 142,298 years of observation. Every worker included in the study had worked in one or other of the refineries for at least one year. The major findings of the study showed that there is some correlation between petroleum exposure and the development of cancer.

In 1977, Blot *et al*[11] reported the results of a survey of cancer mortality in United States counties with petroleum industries. Mortality in the PIC was significantly higher for all cancers combined than in control countries. The largest ratios were for cancer of the nasal cavity and for lung cancer. In addition, mortality was significantly higher for cancers of the skin, testis, stomach, and rectum.

In spite of this known association between petroleum pollution and cancer, Nigerians are daily and constantly exposed to petroleum pollution, be it at the refineries or at the big oil depots located in several parts of the country (Fig. 4) or petrol filling stations or servicing stations (Fig. 5) or mechanical workshops scattered all over the country (Figs. 6 and 7) or on our roads. Are Nigerian petroleum products different from the American ones? Experiments we carried out on superblend petrol have shown it to be highly carcinogenic in rats A preliminary survey of health harzards of petrol station attendants and of motor vehicle mechanics in Oyo and Ondo states of Nigeria showed some significant biochemical and haematological abnormalities.[12] An important observation was the finding of a high incidence of skin dermatitis among motor vehicle mechanics. A typical example of this is shown in Fig 8. These dermatitis are known to be precancerous, and we have already recorded three cases of cancer of the skin among motor vehicle mechanics.

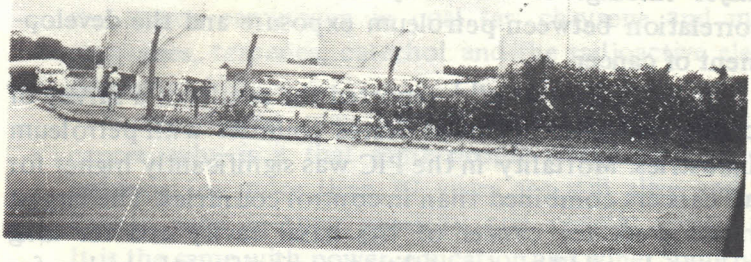


Fig 4 – An oil depot

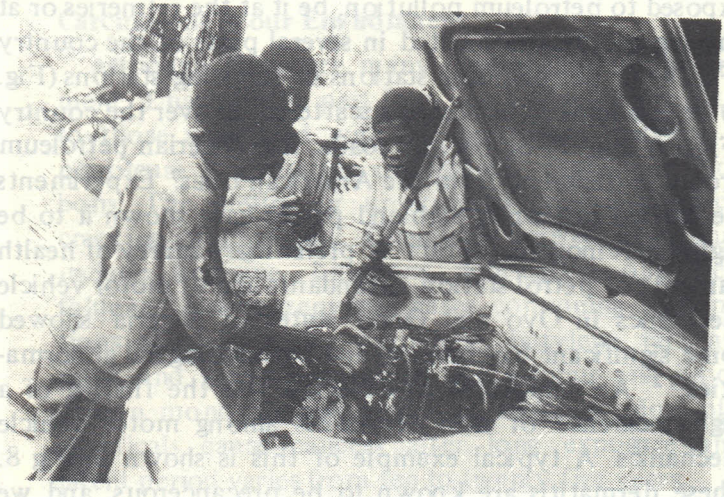


Fig 5 – A motor vehicle servicing station

Figs 6 & 7 – Mechanical Workshops.

Fig 8 – A motor mechanic with dermatitis

We have also carried out preliminary investigations of health hazards of workers in one of our big oil refineries.[13] Although no cancer was found among the workers at the time of the survey, there are indications that the incidence of cancer will rise among them some years from now following prolonged exposure.

Cancer and Heredity

It has often been said that one cannot escape his heritage. It is the same with cancer. A person's biological inheritance in many ways can influence his susceptibility to the effects of cancer-causing factors, and consequently his chances of developing one or another type of cancer. This genetic predisposition to cancer may be determined by such things as inherited immunological defects, hormonal patterns, enzyme deficiencies, bone abnormalities etc.

A survey in Nebraska[14] showed that in families where two immediate relatives had cancer, the risk to others in the immediate family rose to 16.3 percent and it increased to 27.4 percent for persons with three or more relatives who had cancer.

In study of childhood cancers it has been found that brothers and sisters of youngsters with leukaemia, brain tumours and sarcomas seem to face a somewhat greater than expected risk of developing these cancers themselves. In studies of identical twins, it was shown that if one twin develops leukaemia, the other has a one in five chances of also developing the disease within two years compared with the usual incidence of one in 20,000.

Also studies have revealed that breast cancer runs in families. The families of several hundred breast cancer patients had been studied. It was found that if the original patient had cancer in only one breast the risk to her relatives is only slightly higher than that faced by women in the general population. However, if the cancer affected both breasts, the relatives' risk is five-and-a-half times higher than it would otherwise be. If the cancer was both bilateral and occured before the patient reached menopause, her relatives, risk is nine times higher than expected. In women under the age of 40 whose sister and mother both had breast cancer before menopause, the risk is forty-seven times greater.

What Cancer is not Caused By

I have been speaking about things that cause cancer. I think that it is also important for us to establish certain misconceptions about the cause of cancer. There is a popular myth that cancer represents the wages exacted by sin, a punishment for some wrongdoing, real or imagined. There is absolutely no evidence to support the idea that cancer

is the penance people pay for moral lapses, evil thoughts or criminal acts. Even cancer of the cervix which is more common among prostitutes and promiscuous women is not just desserts for moral turpitude: rather it is associated with sexual activity, which most of us engage in from time to time.

Sometimes women think that breast cancer results from being bumped or bruised on the breast or from sexual stimulation and manipulation of the breast and nipples. Since breast cancer is the most common cancer in women and since getting bumped or bruised on a protruding part of the body is extremely common, these two phenomena are more than likely to happen to the same woman. But that does not mean that one caused the other. There is no evidence to even suggest that injuring the breast or manipulating it increases the risk of breast cancer.

V. TREATMENT OF CANCER

The current, proven methods of treating cancer are by surgery, radiotherapy and chemotherapy. Surgery and radiotherapy are both capable of cure in favourable circumstances and both able to relieve symptoms when cure is no longer possible. Cure is a word which must be used circumspectly in relation to cancer for there is no way of being absolutely sure that all cancer cells are eliminated by any form of treatment. As is well known, in certain cancers, secondaries may declare themselves fifteen or twenty years after an apparent cure. The approach to cure can only be understood in terms of the percentage of patients free of clinical disease after treatment. For convenience, the survival rates are usually quoted at intervals of five years, so one speaks of five-year, ten-year, and fifteen-year cures. The accepted sure way of "curing" cancer is to remove it in its entirety.

Although surgery, radiotherapy and chemotherapy are the proven methods of treating cancer, there is a new method known as immunotherapy which has engaged my mind for some time now. In the following paragraphs, I will endeavour to let you know the present position of this new method of treating cancer.

Immunotherapy of Cancer

Armed with the data demonstrating the role of impaired immunological responses in cancer causation, the possibility of altering the course of cancer by manipulation of host defense mechanisms has become increasingly attrative to immunologists and to physicians charged with the care of these patients. The first nonspecific immunostimulant to be demonstrated was bacillus Calmitte-Guerin (BCG). There is epidemiologic evidence of decreased incidence of lymphomas and leukaemias in countries with routine BCG immunisation programmes. It was also found that vaccination of human populations in 1949 in the province of Quebec in Canada led to a reduction to about half the number of death from leukaemia fifteen years later when compared with the non-vaccinated population. The above epidemiological data led to the use of BCG, in clinical trials, for the treatment of cancer. But the results were not encouraging. This led to the search for other agents.

It was observed about 10 years ago[15] that extracts of human peripheral blood leukocytes could transfer cellular immunity from immune donors to non-immune recipients. This was called biologically active material transfer factor. Transfer factor is a small molecular weight (10,000) soluble dialysable, lyophilizable product of lysed peripheral blood leukocytes whose biological activity is not destroyed by DNAse or pancreatic RNAse. It is prepared from lymphocytes of highly sensitized donors.

On the anti-cancer effect of transfer factor, it has been reported that 7 out of 9 patients receiving it had 50% reduction in cancer mass. There was also observed a transient decrease in tumour size in 1 out of 4 patients with recurrent breast cancer.[16]

Here at Ife, we have been interested in the use of thymosin and interferon in the immunotherapeutic treatment of cancer. Thymosin was first isolated from calf thymus by Goldstein *et al* in 1966.[17] Chemically, thymosin consists of a family of mostly small acidic polypeptides with molecular weights ranging from 1,000 to 15,000. It is thought that biological potency of thymosin may be due to more than one of these peptides acting either in concert or individually on various subpopulations of T cells. Goldstein and his colleagues have now treated more than 110 cancer patients with thymosin in doses ranging from 1-250mg/m^2. Patients have been treated from days to more than 18 months. Goldstein and his team observed some clinical responses in some of these cancer patients.

At Ife we have carried out experiments on the effects of thymosin on T-lymphocyte rosette formation in histologically proven 14 cases of hepatocellular carcinoma, 21 of Burkitt's lymphoma, 13 of Hodgkin's lymphoma and 15 of cancer of the breast. Thymosin fraction 5 was found to cause a significant increase in T-lymphocyte rosette formation in patients with Burkitt's lymphoma and Hodgkin's disease but not in patients with hepatocellular carcinoma and cancer of the breast.[18] We believe therefore that thymosin may be effective in the treatment of Burkitt's lymphoma and Hodgkin's disease. Following the publication of these results we have got offers from two firms, one an American and the other Swedish, willing to collaborate with us on clinical trials involving the use of thymosin and interferon in the treatment of Burkitt's lymphoma. Work will soon start on this.

VI. PREVENTION OF CANCER

In these last paragraphs I want to try and answer an important question: Can Cancer be prevented? The natural history of cancer as a clinical disease suggests that the best approach to its containment would be first prevention, and second early diagnosis and proper treatment. Yet today the desirable goals of prevention and early detection have not been reached. Each premature death from cancer is a personal tragedy. Each preventable death is a national reproach. Each year more and more such deaths are occuring for the pace of science is bringing them more within our reach but the pace of application allows them to slip through our fingers.

Perhaps to understand what preventive measures can be available we need to briefly review the natural history of cancer. First there is an interaction between some inciting factors and stimuli (chemical, physical, nutritional or biological) and the patient's organism. This is a latent dormant period when nothing seems to be amiss. Then a change begins to appear in the tissues, in a localised site, and one speaks of cancer *in situ*. The tissue changes are quite identifiable in the laboratory but the patient is still well, showing no clinical symptoms of illness: he is asymptomatic. Finally the clinical horizon is reached, the cancer is localised to an organ, signs and symtoms are identifiable and the disease becomes discernible.

Surely, therefore preventive measures should of necessity include:

a. Avoidance of known and potential carcinogens,

b. Screening for early detection,

c. Public education, and

d. Genetics counselling and population genetics.

Avoidance of Known Carcinogens

Since cancer has been linked with cigarette smoking, exposure to ulta-violet light and nitroso compounds, chewing of betel and environmental pollution, many cancers will not occur if these are avoided.

Screening

There is no better example of the value of cancer detection than the results of mass screening programmes for cervical cancer organised in British Columbia, Canada in 1950. To date about 75 per cent of the female population has been examined and cancer of the cervix has declined significantly.

As at now no simple general screening test for cancer is possible and the search must of necessity be painstaking on an organ to organ basis Lung cancer cannot be detected without a complete X-ray of the chest, early cervical cancer cannot be revealed without a Papanicolaou smear, early rectal or colonic cancer without a protoscopic examination, or early oro-pharyngeal cancer without an examination of the larynx. Except for the pap smear which is so simple that it is a part of the routine of a general examination for the majority of doctors, these tests are not and often cannot be given by individual physicians.

Taking a complete medical history and running a complete physical examination of a patient by a physician at least once a year is important. Such routine physical examination for early detection should include then:

a. Examination of the pelvic organs by the Papanicolaou smear technique.

b. An oro-pharyngeal examination

c. A routine chest-X-ray

d. A proctosigmoidoscopic examination

e. A blood examination for abnormal cells and the presence of Oncofoetal antigens and other biochemical tumour makers, which we can do here at Ife.

In a population, the size of Nigeria, individual screening tests defy the present ability of doctors to conduct them and of patients to pay for them. The maintenance of health or the prevention of illness, must therefore become a concern of the community, of the state and of the nation; the treatment of cancer can remain the responsibility of the individual physician on a patient-to-doctor basis.

Public Education

Public education plays a key role in cancer prevention and early detection. Accurate information must be spread about cancer and particularly about the hopeful prognosis on many forms of cancer when detected and treated early.

The public must be aware of the following warning signals on cancer:

a. Any persistent lump of thickening in tissue, especially in the breast, lip or tongue.

b. Any irregular bleeding or blood-tinged discharge from any body opening, including a nipple.

c. Any sore that does not heal.

d. Persistent indigestion or loss of appetite especially in people over forty years of age.

e. Sudden or rapid changes in the form, appearance or rate of growth of a wart.

f. A persistent change from normal in bowel action.

g. Persistent hoarseness, cough, soreness deep in the throat or difficulty in swallowing.

The importance of being aware of these warning signals and acting on them is well illustrated in the results of

breast self-examination which has been extensively publicized by the American Cancer Society in its teaching films and through the mass media. Ninety percent of breast cancers are detected by patients themselves in probing for lumps with their own fingers. Verification of the nature of the lump and its appropriate treatment of course requires medical supervision. The Nigerian Cancer Society, sometimes ago embarked on a programme of public education about cancer on television, but this was short-lived. A disadvantage of television advertisements in this country is that population at risk hardly ever benefits from them.

Genetic Counselling

Cancer is an increasing threat to the life and health of children. The seeds of cancerous traits are commonly sown before birth through a change in a single gene or even an inconspicuous change in the growing embryo which may for instance have been exposed to x-rays. Such genetic changes are passed down from one generation to another.

Many "cancer families" have been identified by geneticists through the accurate mapping of family trees over several generations. These cancer families have a high incidence of cancer in many sites and cancer tends to appear among them at an early age. Parents who have suffered the loss of one child from cancer naturally wonder whether it is safe to have more children. This raises the question of genetic counselling and all its profound implications. Genetic counselling should never be used in a manner capable of arousing fear of cancer but as the most delicate theoretical weapon.

What is known of genetics and cancer can serve to reassure healthy parents with an affected child. It is safe for them to have more children unless they are clearly a cancer family in which case they should be warned that a

new child in their family would face the risk of being affected by cancer too. Persons who have survived operation for embryonic cancer in their own childhood, who have survived retinoblastoma or Wilm's tumour should probably make the decision not to have children.

The parents of a mongol child should be informed that leukaemia is frequent in such children. And if the parents already have two or more affected children (either with mongolism or leukaemia) their chances or having a third or fourth child suffering from these abnormalities are extremely high and they should be so advised.

VII. ROLE OF GOVERNMENT IN THE FIGHT AGAINST CANCER

From the foregoing, it will be appreciated that the fight against cancer should involve not only physicians but the whole community and the various State and Federal governments. If the fight is to be successfully waged, there must be co-ordinated efforts between these various groups. What I will like to recommend is the setting up by the Federal Government of a National Comprehensive Cancer Centre to be manned by highly competent personnel.

Such centre should integrate patient care, research, and education under one management. The goal is to translate the results of research to multidisciplinary care of the cancer patient and ultimately, through education, to the medical profession and the public. The centre should strive for a well-balanced programme of patient care, research and education. Included in the commitment should be a cancer registry to enable us assess the incidence of cancer in our society, patient follow-up system, rehabilitation, cancer prevention and earlier detection programmes. We must remember that the fight against cancer is a tough one. Fig 9 is an allegorical presentation of the fight between man and

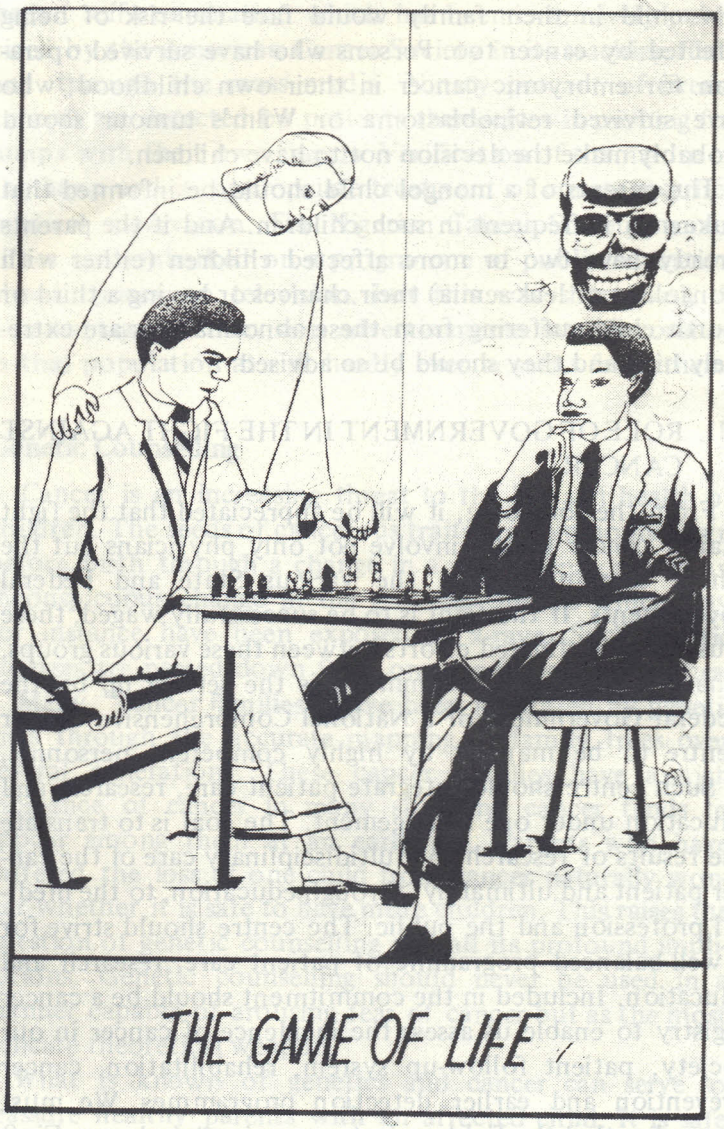


Fig 9 – An allegorial presentation of the fight between man and cancer

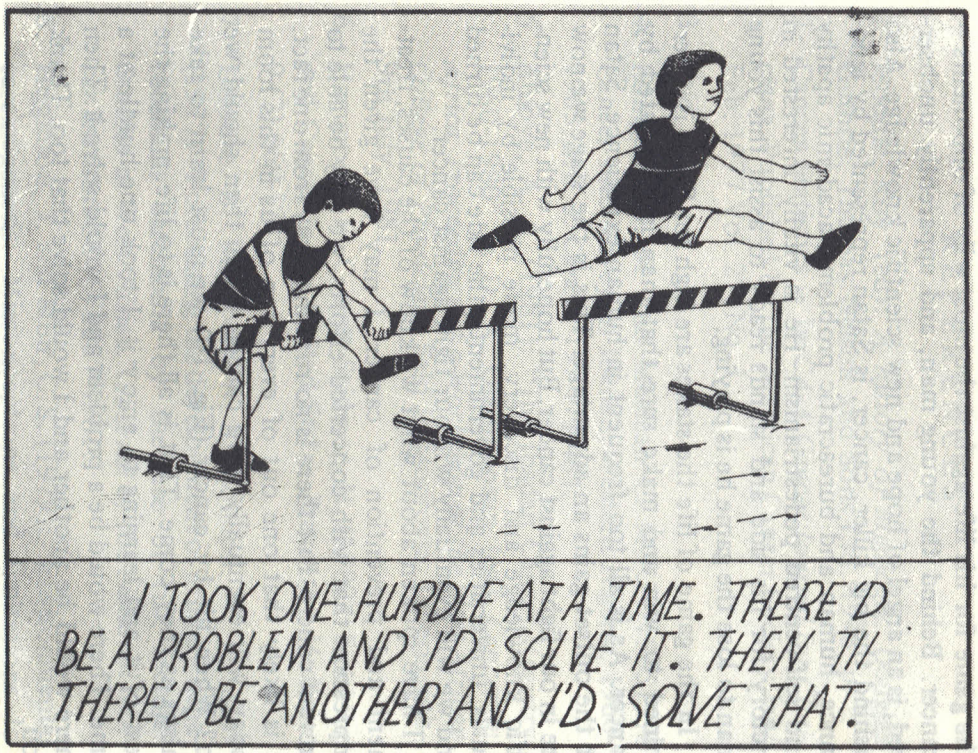

I TOOK ONE HURDLE AT A TIME. THERE'D BE A PROBLEM AND I'D SOLVE IT. THEN TH THERE'D BE ANOTHER AND I'D SOLVE THAT.

Fig 10.

cancer be it biological or moral. A young man is playing the game for his life against the most wily of opponents – cancer. Behind the young man, and apparently unobserved, is an angel of hope and new scientific knowledge. Also behind the big killer, cancer, is Satan represented by ignorance, human and bureacratic problems, academic apathy and self-centred pedestrianism. He is vitally interested in victory for his side and stands ready to assist this young man to lose the game he is playing.

In the game of life the stakes are high for Satan is determined to win and make sure that man is eliminated by cancer. As is all too frequent in human experience, Satan at the outset gains an advantage. This is the stage we now are in our fight against cancer. But hopefully with new scientific knowledge and discovery, made possible by individuals, universities and governments, the tide can be turned and we will eventually win our fight against cancer.

I have spoken about what we know of the causes, treatment and prevention of cancer. I may have given the impression that with concerted efforts, we may be able to prevent cancer. But there is no running away from one fact. It is likely that one out of every ten of us in this room today will eventually have cancer. What then should we do? When hit by cancer (Fig. 10) we must learn to take things as they come. That is all there is to life, making the best of it and learning to enjoy it. I took one hurdle at a time. There would be a problem and I would solve it. Then there would be another and I would solve that too. Thank you.

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