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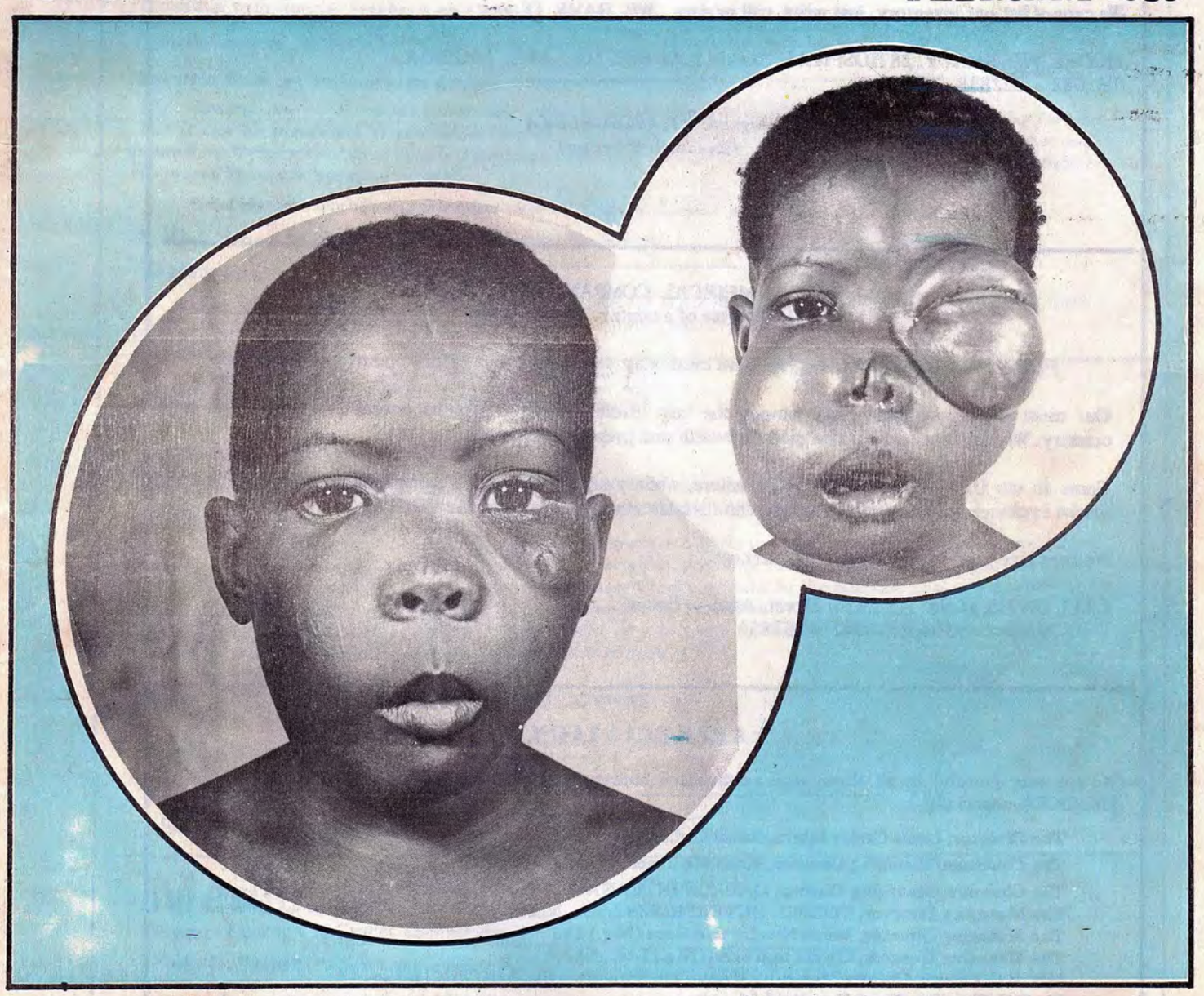

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- Medical News
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MEDIKKA

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IRNAL OF UNIVERSITY OF NIGERIA MEDICAL STUDENTS ASSOCIATION

VOL. IV Nº 1

Editorial Opinion:

WE CAN MAKE IT

In this edition of MEDIKKA, which bears an International Standard Serial Number (ISSN: 0331 – 1643), there is much emphasis on cancer, a disease that is posing danger and may pose a great threat to life in the near future (especially in developing countries like Nigeria). The edition aims at creating a high index of suspicion in order to reduce the high morbidity and mortality pattern of cancer in our environment. This, it achieves by digesting the theme (NEOPLASIA WITH SPECIAL EMPHASIS ON CANCER) for the interest of the general reader in a special section – GENERAL FEATURES. The interests of medical practitioners, students and allied professionals are specifically represented in other sections of the journal – SPECIAL FEATURES, NEWS, INTERVIEWS and MEDIBITS. Simple diagrams and cartoons have been annexed to some articles to make some relevant points clearer to our readers.

The front cover design clearly dispels the common public belief that cancer is untreatable – the pictures are of a Burkitt's lymphoma patient (before and after treatment at UNTH).

We, in MEDDIKA, believe that Nigeria needs indigenous medical journals that can compare favourably with established journals elsewhere in terms of the pragmatic value of their contents. Such journals are to provide an avenue for sharing experience and exchanging ideas both locally and internationally. They can also help to harness the numerous contributions of local scientists and foster cumulative growth of knowledge which will create room for the growth of indigeneous affordable technology. This is very vital for the success of HEALTH FOR ALL BY THE YEAR 2,000.

Although there have been indigeneous journals, their production has been intermittent and irregular. MEDIKKA, for example, has had a chequered history since its first appearance in 1975. It appeared for 5 years consecutively (1975 to 1979), disappeared between 1980

EDITORIAL POLICY

MEDIKKA is an annual medical journal published by the University of Nigeria Medical Students' Association at the College of Medicine of the University of Nigeria, Enugu Campus, Nigeria.

The Editorial board accepts original articles, subject reviews, case reports and research work on problems relevant to Nigeria and other African countries. Articles should not exceed 3,600 words. They should be well supported with tables, figures and graphs where necessary. Each article should with a precise but comprehensive summary or abstract.

Articles which have appeared in other journals will not be published in this journal. Also, each article must have a title, author's name with his full address, qualification and the institution in which the research was carried out. All references should follow the Vancouver system.

The Editor reserves the right to shorten and correct the articles received (in consultation with the Editorial Adviser and the Editorial Consultants) without altering the subject matter of the articles. He does not bear responsibility for any ideas expressed by the contributors in the articles.

The contributors of articles may claim off prints at a cost (including postage) to be determined by the Editor—in—Chief.

All manuscripts should be typewritten with double spacing on one side of the paper only. Manuscripts and all correspondences should be sent to:

The Editor—in—Chief,
MEDIKKA
c/o The Provost's Office,
College of Medicine,
University of Nigeria,
Enugu Campus,
Nigeria.

Articles or materials for publication in the next issue (Vol. IV No. 2) should reach the Editor on or before 31st October, 1989.

and 1984, reappeared in 1985 and 1986, remained dormant from 1987 to 1988, and reappears in 1989. The major problems were lack of a pool of articles (for publication) and lack of funds. It is hoped that the present edition of MEDIKKA will herald an era of regular publication of high quality journals of international standard in Nigeria.

WE CAN MAKE IT work if we review the neo—colonial spirit of our academic evaluation scheme that acclaims outside publications more than local ones. Does the quality of a work reside in where it is published or in the pragmatic value of the issue raised or discussed? Granted that medicine, as an art enlightened by science, has universal principles, does this in itself imply that recent developments or findings must be presented to the world only through the "established windows"? Besides, while publication in overseas journals may be based on the extent to which a work attends to a medical problem with universal import, provision for works with predominantly local import may be very lean – what then becomes the fate of such works? Assessment of our academics should be based not only on the number of works published in established journals (outside Nigeria) but also on the number of well meaning works published locally – this will encourage our academics to groom their society with their wealth of knowledge. They owe this as a duty to the society which nurtured them.

WE CAN MAKE IT with the support of the rich and the wealthy in our society, who also owe it as a duty to the society, to encourage the academics in their noble role, by sponsoring the publication of high quality indigenous journals. William Shakespear says that "to climb steep hills requires slow pace at first". However, it must be realised that as Alfred North Whitehead noted, "periods of quiescence are seldom prolific of creative achievements, (hence) mankind has to be stirred up"

Francis O. Chukwuani, B.Phil. Hons. (Rome).
Editor—in—chief, MEDIKKA.

ACKNOWLEDGEMENT

We are grateful to our editorial adviser, Prof. C.H. Anyanwu (Head, Department of Surgery, UNTH) for his invaluable advice and untiring efforts in the production of this edition of MEDIKKA. We are also indebted to all our editorial consultants for their advice and assistance.

Finally, we thank our beloved University of Nigeria Medical Students' Association, who under the peaceful and progressive administration of Mr. Kennedy Ononaeke (1987/88 session), set the pace by publishing this special edition of MEDIKKA. We hope for a bright future for MEDIKKA in the dynamic administration of Justice C. Nwosu (1988/89 session).

Guest Editorial:

CANCER RESEARCH BY MEDICAL STUDENTS

PROF. WILSON I. B. ONUIGBO
MD, FRCPATH., Department of Morbid Anatomy,
University of Nigeria, Enugu Campus.

I was glad to receive the invitation of my student, Mr. Okwudili Chukwuani, the editor of *Medikka,* to contribute a guest editorial for this issue. The numerous manuscripts are a feast in themselves, the published articles cannot but be worthy of consumption by general readers, students, medical practitioners, and other professionals, especially as the main theme concerns cancer.

I am not new to *Medikka*[1]. During my first academic journey to this Medical School (April 1977 to June 1978) as Visiting Professor and, Head of the Department of Morbid Anatomy, the then Editorial Board invited me to speak on "Pathophysiology" at a symposium on Tuberculosis. I referred to the biblical story of the seven sons of Sceva who attempted disastrously to cure a mad man. Alas, the man replied, "Jesus I know, and Paul I know; but who are you?" Accordingly, borrowing even from a mad man, I began my assignment by saying, "Pathology I know, and Physiology I know; but what is Pathophysiology?"

I am not new to cancer research during medical studentship. When I was in my final year at the University of Glasgow, I published "Some observations on the spread of lung cancer in the body" in the prestigious *British Journal of Cancer*[2]. The study was based on (a) reading through and analyzing thoroughly one thousand lung cancer postmortem records, (b) finding a significant relationship between site of origin of the lung cancer and side of invasion of the adrenal gland, and (c) supporting my new theory of cancer dissemination with 39 references to theses, books, and journals published between 1896 and 1957, the year of my own publication.

Naturally, I am still interested in cancer research. However, other fields have crept in! One of them is scientometrics. Thus, I have published several papers on the patterns of reprint requests (RR). These writing/led John Swales, the editor of *English for Specific Purposes,* to refer to me as "the only active researcher that I have traced in the RR area"[3]. My activity in the RR area has convinced me that reprints have a "tracing power" of their own. For instance, I used RR in 1983 to trace the "brain drain" phenomenon as it applies to India[4]. In the present guest editorial, let me use this same power to paint the picture of cancer and related researches carried out and published by medical students in different parts of the world. The fifteen examples are selected from the thousands of reprints in my mini–library!

Patrick Marabella[5], a premedical student at the University of Buffalo, New York, was listed as the third of four authors who published clinicopathological studies on lung cancers of the small cell type. They concluded that the outlook for such cancers is so grave that postponing the death of sufferers to more than a year is the "immediate therapeutic goal".

Two years later, in another paper[6] written when he had transferred to the State University of New York, he was the first of two authors. Their publication was a preliminary report on using lung cancer extract as a skin test for determining patients likely to show longer survival times.

Still on lung cancer, student D. Harrison[7] was the first on a list of three authors based at the University of Western Ontario, Canada. He was described as "Summer student, supported by University of Western Ontario research grant, M079A 1." They showed that biopsy of mediastinal lymph nodes is a definitive staging procedure for lung cancer.

Still in Canada, student Clifford Blais[8] was the third of four authors based at McGill University. They reviewed lymphangioma in children as regards embryology, classification, clinical presentation, and treatment, exemplifying with eight case reports.

Remaining in Canada but going to Queen's University, Kingston, we find student P.G. Garrett[9] being listed last among four authors. They wrote that only 200 cases of malignant lymphoma of the thyroid gland had been reported from 1960 and presented four case reports.

Back to USA, student Harold Brody[10] of the Medical University of South Carolina was a sole author. He reviewed the etiology of colonic cancer with 9 references. In his own words, "The geographical variations in the incidence of carcinomas of the colon seem to be correlated with the fat content of diet. There has been a rise in incidence in Negroes following adoption of White food habits. Negro slaves had as little cancer as Africans today. Thirty years ago, when more maize was eaten by American Southern Negroes, there was only half the incidence of cancer, this difference today has vanished."

Student Andy Ruth[11] of the University of Minnesota co–authored with a surgeon two case reports on the relatively rare condition of lipomatosis of the ileo–caecal valve. Curiously, both cases were incidental findings during routine diagnostic workup.

Lee Skandalakis[12], described as "Third year Medical Student" of Emory University in Georgia, was the leading author who with three others studied axillary lymph nodes removed during breast cancer surgery. They advise that "the pathologist should section, in addition to the palpable nodes, at least five less fatty areas of axillary tissue taken at random." Curiosity leads me to speculate that the one author named John Skandalakis and described as "Chris Carlos Professor of Surgical Anatomy and Technique" was probably the father of the student author!

From the Southwestern Medical School in Texas, a female student, Cheryl Szpak [13], was the leading author. There were two associates. Their observations centred on the demographical and geographical incidence of cancer of the lip and oral cavity. Among other things, they found a *significant* decline in the incidence of oral cavity cancer and a *slight* decrease in lip cancer over the past two decades.

From the University of North Carolina, student John Kemodle[14] was listed second among three authors. They had tackled the problem of factors which influence the occurrence of advanced cancer of the neck of the womb. They enthused: "Innovative ideas applicable to a particular city or community are needed to reach patients who are particularly at risk for invasive cervical cancer."

Crossing the Atlantic, we go to the United Kingdom. There, we meet a medical student with the foreign name, A.Y.C. Chan[15]. He or she was the second of three authors who calculated the cost of postoperative complications following major abdominal surgery, including elective resection for large bowel cancer, in the University Surgical Unit of the Royal South Hants Hospital.

Also with the foreign name of H.S. Pandha[16] was a medical student at the University of Birmingham. He or she occupied the third position in a list of four authors whose work was on cancer in blacks, whites and Asians. As their last sentence ran, "It will be interesting to see if the changes in incidence rates seen in immigrants to the USA will be reflected in subsequent generations of Asians and blacks born in the UK as they adopt westernised life–styles."

Coming to mother Africa, student R. Marcus[17] ranked second among three authors at a Teaching Hospital in Johannesburg. They surveyed the characteristics of Mozambican males of the Shanagaan ethnic group who developed liver cancer, taking special note of their dietary habits. Apparently, this cancer has its highest incidence in the world among Mozambicans.

Next, we go as far away as Australia. There, we note that student Michael Ponsford[18] took the second position among five authors working at Monash University. They found that age, skin type, and sunlight exposure are the major factors influencing the prevalence of skin cancers.

Finally, in neighbouring New Zealand, student Gregory Simmons[19], led two other researchers at the University of Auckland to investigate the association between one viral infection and liver cancer. They discovered that Pacific Islanders and Maoris had a higher viral carrier rate and higher incidence of liver cancer than their European counterparts.

What lessons do the above examples teach? First, medical students can publish, in international journals, research carried out alone or with one or more professionals in the field of neoplastic disease. Second, the facet covered may be clinicopathological, experimental, clinical, surgical, etiological, epidemiological, etc. Third, the individual student tends to be incorporated in a working group rather than two or more students. Fourth, males rather than females feature as student associates. Fifth, the student is likely to be listed first, last or in the middle position. Sixth, foreign students take part in researches. Seventhly, student research may be supported by financial grant.

To my mind, the composition of a research team that includes a medical student was ably depicted by Kevin O'Malley[20] who collaborated with a student and my own pharmacology teacher, James Crooks, in a highly cited publication. He wrote thus: "The composition of the team that carried out the work is of interest. Crooks was in the process of setting up clinical pharmacology as a major section in his new department. Duke was an interested medical student hoping to gain experience in research. As a recent medical graduate with relatively little scientific background, I wished to become a scientist and had Stevenson as my mentor. This foursome represented many of the important elements in a medical school – professor/chairman, medical student, medical graduate/research fellow, and scientist, each playing an important role in the venture".

Let me describe such an excellent relationship another way by borrowing from Eugene Garfield[21], who highlighted the remarks of Robert Wilson, past president of the American Physical Society, thus: 'In some major way, the production of scientists is a 'laying of hands' process. It is exposure of young people to older people who care about science, who do research, who have the research fever".

What then are the responsibilities of a teacher? I like the way that this question was answered by Richard Edlich[22] of the University of Virginia Medical School. "The chief responsibility of a teacher in the School of Medicine," he affirmed, "is to create an atmosphere friendly to learning." And he added, "A teacher must be the professor of the open door, easily accessible to students or associates."

In conclusion, I have personally encouraged student research. Indeed, I nurtured with both ideas and reprints some of the articles in this issue of *Medikka*. I would like to draw special attention to the one contributed by Miss Ifeoma Ezekannagha and Miss Regina Amadi. Perhaps, I should have asked them to include my name as the last author! However, according to an Igbo adage, a monkey said that she would only vouch for the foetus in her belly and not for the infant on her back – for the simple reason that the latter might well have plucked a fruit without her knowledge!! To be their co–author, I would have taken more active part in analyzing the records which they so nicely presented. Be that as it may, what remains is to wish them and their fellow students the best of luck in future researches and other endeavours.

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Neoplasia with special emphasis on cancer — an overview

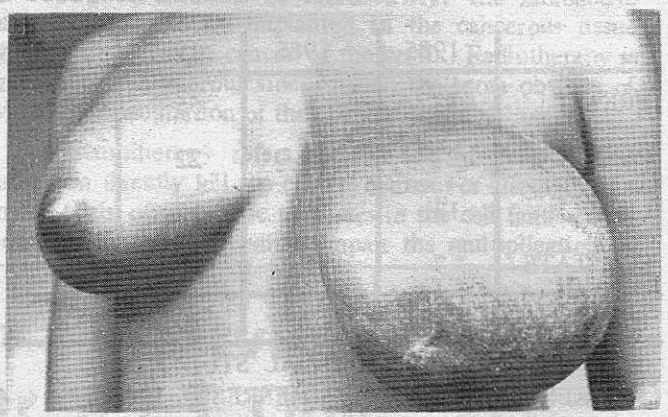
Chinedu Nwigwe, Anelechi Anyanwu and Regina Amadi

It was an early harmattan morning, Mrs. Akweke filled her pot with water from the stream, balanced it on level ground and went back to the stream to take her bath. She splashed some water on her hands and face to attune her body to the temperature of the water, she then dipped her whole body into the stream. She scrubbed her legs, her back and her trunk vigorously. As she finished giving the face same treatment, her hands came to the breasts, and to her surprise, she felt a hard nodular swelling on the left one. She examined it carefully, finished her bath and went home.

She rubbed 'okuma' – a local balm – on the swelling taking it to be a boil. After a week's treatment, the lump still peristed. She showed it to Mrs. Okenwa who advised her to see Awuzie, the native doctor. Awuzie dismissed it as bad blood made a number of incisions and let out some blood. Like an enraged lion, the growth went on rampage. It's size increased tremendously and rapidly and it became large and hard like an unripe pawpaw but with an orange-like skin. Mrs. Akweke became weak, emaciated, ill and sad.

Her son, unimpressed by the local treatment being given to her, took her to a teaching hospital. Cancer of the breast was suspected so the lump was removed (excision–biopsy). After looking at the tissue under microscope (histology), the diagnosis of breast cancer was confirmed. She did not know what it meant but the sound had a mysterious and disquieting aura like a coin dropped into a still of silence. She was placed on drugs but died four months later with confusion and sad hopelessness written all over her face.

This frightening story has acquired varied interpretations. The traditional folks call it bad blood, a curse from the gods etc. Recently, in a television interview, Trad. dr. J.O. Lambo, the National President of Nigeria Association of Medical Herbalists claimed that cancer and AIDS are extraterrestial in origin. He said cancer was brought by astronauts from the moon and so would require metaphysical intervention before it could be cured. Considering the historical fact that cancer existed long before the Wilbur brothers made the first planes, the cogency of Trad. dr. Lambo's assertions becomes highly debatable. However, neoplasms have constituted a great challenge to the vital spirit and goals of science. Today, neoplasms are said to be abnormal increase in the number and size of cells, an uncontrolled useless growth. Dr. J.L.I. Odili, a Consultant Oncologist and Immunologist at UNTH says about these cells. "they multiply and grow irrespective of the growth regulatory mechanisms of the body. They seem to grow wild and unchecked....." But not all neoplasms are so aggressive. While the benign neoplasms grow slowly and are restricted within capsules, the malignant ones know no bounds and are called "Cancers". This non–restriction to a boundary which is of great interest to pathologists is masked by their more obvious characteristics; they do not discriminate among tissues affected, and they cause immense suffering and death.



A large fibroadenoma: a neoplastic condition of the breast. Curtesy of Prof. O. Ojukwu, Dept. of Surgery, UNTH.

Kaposi's sarcoma: a malignant growth affecting the skin. Curtesy of Dr. Amamilo, Dept. of Orthopaedic Surgery, UNTH.

Cancer, the Latin word for crab, must be as old as the cell itself. Actually, it has been discovered in the fossils of prehistoric monsters that inhabited the earth before man. The oldest known neoplastic specimen is in the Natural History Department of the British museum – a fossil bone of a dinosaur approximately 80 million years old. The oldest example in man is found in the fossil remains of a human jaw dated 50,000 years and stored in the same museum. However, the earliest description of cancer of the breast and probably of cancer in any form is credited to Egyptian Physician Imhotep in 3,000 BC and is recorded in the Edwin Smith Surgical Papyrus under case No. 39 'Bulging Tumour of the Breast'.

There was a general belief that the Negro race was less prome to malignancy than the caucasians. Sharp (1923) observed the rarity of cancer in Nigeria whilst Blair claimed that he never encountered a malignant

CHINEDU NWIGWE, ANELECHI ANYANWU AND REGINA AMADI are 5th year medical students at the College of Medicine, University of Nigeria, Enugu Campus (UNEC).

tumour in his 22 years of practice in Nigeria. In 1976 at UNTH 4790 cancer patients were seen. In 1986, the proliferation of hospitals notwithstanding 2951 patients were seen. Considering these rates of incidence in our hospital now, it can be infered that non–presentation of patients was the cause of the low record of cases in Nigeria in the early part of this century. However studies done in UNTH on yearly presentation of cancers (between 1985 and 1987) shows an alarming rise in incidence.

DISTRIBUTION OF HISTOLOGICALLY REPORTED CASES OF FOUR COMMON CANCER – TYPES AT UNTH N = 707

	1985	1986	1987	1988
BREAST	53	46	55	40
CERVIX	27	28	22	33
LIVER	13	15	13	14
PROSTATE	7	11	10	13
TOTAL	100%	100%	100%	100%

– Curtesy of the MEDICAL STUDENTS RESEARCH SOCIETY (MESRESO), UNEC.

This alarming incidence of neoplasms has fueled the urge to research into the cause of this disease. But this search is not new. In 1775 Percival Pott a British Surgeon described the first occupational cancer, scrotal epitheliomas in chimney sweepers. His accurate observation triggered off volumes of theories on and experiments into the causation of cancer.

Two Japanese doctors Yamagiwa and Ichikawa started experiments on rabbits to confirm the 'irritation theory' which emanated from the chimney sweep observation. They painted rabbits' ears with coal tar over a period. First there was thickening of the skin, then warty growths – some had stems and assumed the name stemmed papillomas Later the growths took on irregular and bizarre shapes, invading the tissue below and finally spreading to other parts. This experiment conducted in 1915 became the first scientific proof of irritation as a factor in the causation of cancer and produced the first experimental tumours. Encouraged by this work, several hypotheses of cancer – causing agents swept through the scientific fraternity. In 1930, 1,2,5, 6 benzanthralene contained in coal tar became the first pure chemical shown to induce cancer. Six years later, Dr. Kinosita discovered the carcinogenic effect of butter yellow. Only recently, Prof. Okonkwo, a professor of Pharmacology at UNTH discovered the presence of aflatoxin, which is implicated in liver cancer, in mouldy groundnuts. Other chemical carcinogens include nicotine in tobacco and several other industrial chemicals. But the nagging question is whether it was merely irritation or whether these chemicals had more intricate machinations in the cells.

A major landmark in this search for a definite cause was the arrest of virus as one of the culprits. Rons discovered that the cause of chicken sarcoma was a virus. Since then, Bitner (1938), Burkitt (1958) have incriminated viruses as the causative agents of breast cancer and Burkitts Lymphoma respectively. This major breakthrough by Rons in 1911 reopened the debates on the possibility of cancer being infectious or inheritable.

Miss Maud Slye, an American professor interested in the inheritance of psychological problems was a great proponent of inheritance of cancer. After her numerous researches on mice she observed that, 'cancerous cells lacked the differentiating mechanisms which shapes and controls the growth of normal cells'. But Dr. Warthin and later Dr. Hansen used the family pedigree for their study and concluded that "while susceptibility to cancer itself was not inherited in the Mendelian sense, there was strong evidence that specific organs of the body might have a predisposition to carcinoma". On the infective theory of viral neoplasia, Dr. Odili dismissed the idea saying 'during the process of transformation of normal cell to a malignant cell, the virus genome becomes incorporated into the normal cell genome to form a tumour specific antigen. This virus which can replicate and as such infect another cell'.

The introduction of X–ray in the 19th century introduced another set of defendants in the case. X–rays and other nuclear rays, even ordinary ultraviolet rays, are strongly suspected of causing cancers of blood tissues and skin. However the real absolute problem in the cancer cell still remains obscure or elusive.

Dr. Greensteins' Abhormal Catalase Action' and the theory of 'Misplaced Embryonic Tissue' have all failed to give a satisfactory and definite explanation of cancer. Dr. Odili affirms this by saying 'if anybody pinpoints the cause of cancer, the person will of course receive the Nobel prize. and if we know the actual cause, naturally that will lead to specific treatment'. For now this hope has not materialised thus letting this monstrous disease rear its ugly head defiantly.

Though scientists have not discovered what goes wrong in a neoplastic cell, they have at least succeeded in naming, characterising and describing the various forms of the disease. Different neoplasms have been conferred with colourful and at times frightening titles. Sarcomas are used to describe the malignant neoplasms arising from the middle layer (mesoderm) of the embyonic germ tissue while carcinomas are those from the inner layer (endoderm) and outer layer (ectoderm) i.e. from the epithelial tissue. Examples are osteosarcoma (bone cancer), liposarcoma (fat tissue cancer); others are basal cell carcinoma, squamous carcinoma and so on. The benign neoplasms are called osteomas, lipomas from bone and fat respectively.

Neoplasias, not always content with their accomodation, tend to invade and intrude into other structures of the body. Some invade neighbouring tissues directly (local spread) – this is common with the benign neoplasias. Others travel long distances through the blood, lymph or open spaces to impose themselves on largely unconcerned tissues. They then occupy and multiply in this new environment inconveniencing the tissue and the whole body. The lymph nodes in their bid to stop this visitation of death become a very common host to cancerous cells. This mode of spread is called metastasis. In this way, breast tissue can grow in the liver giving a false impression that the liver tissue is growing abnormally – this type of cancer is called secondary cancer. This is in contradistinction to an original abnormal growth of the particular tissue which is called primary cancer of that organ.

Cancer thus is really a rebellious contrast to the fine

order in nature; it is without form, symmetry or balance. Ugochi Amadife, an undergraduate and native of Udi says "in my place, it is dreaded because of its acclaimed incurability." The morbidity and mortality caused by cancer tends to give credence to this belief.

Neoplastic growths can block the uterine cavity, the airway, obstruct the gut or bladder opening. Apart from these gross disturbances, cancer sets off a discordant note in the body's homeostatic symphony. The intestinal and renal cancers disrupt the waste management system of the body and lead to the dumping of intolerable amounts of toxic wastes in different tissues. The leukemias – cancer of white blood cells – make the white blood cells grow like marshmallow thus crowding out the oxygen–carrying red blood cells. This essentially cuts off the energy supply to the tissues making the individual weak, pale and ill.

Gruelsome though these mechanisms are, it cannot be said that cancers are uncontrollable. Dr. Odili says; "the problem in this country is that patients do not see the doctor early enough. Also most of the the drugs in 'Ogbete Market' are fake." In fact, he is just highlighting the point that the scientific world is doing a lot to wipe away this scourge.

After searching its armamentarium, medical–oriented science has come up with four main weapons of attack to curtail the march of this devastating enemy. However, definitive treatment has not yet been achieved. The oncologist, Dr. Odili affirms: "I would start by saying that effectiveness of cancer treatment lies in early diagnosis... I would also really talk of cancer control because the disease is such a difficult thing – you may believe you have treated a case, 3 – 4 years later, it may reappear".

The 'control' methods are surgery, radiotherapy, chemotherapy and immunotherapy. Psychotherapy and Trad. dr. Lambo's metaphysical cure have not made any significant practical impact.

Surgical removal of tumours seems simple and has a tangible effect. The mass is excised and the tumour is no more there. Surgery however is useless in blood cancers e.g. leukemias, multiple myeloma and also in cases where multiple masses are distributed all over the body e.g. Hodgkins lymphoma. Mechanical manipulation of the mass can cause the spread of cancer cells (micrometastasis).

Radiotherapy is administered by exposing the tumour to controlled amounts of radioactivity. The radioactive material can also be implanted in the cancerous tissue where suitable as in cancer of the cervix. Radiotherapy is fraught with numerous side–effects, the most obvious of which is imflammation of the skin (dermatitis).

Chemotherapy refers to the use of drugs. These drugs can directly kill the cell (cytotoxic) or effect a break in the chain of metabolic processes in the cell (anti–metabolite). The cytotoxic drugs impair the multiplication of cells by interfering with enzymes and protein in the cell. The drug kills about 90% of the cells of the tumour and this concept is called the 'Fractional Cell Kill' concept. The principles of chemotherapy include continuous single agent, cyclical, intermittent high dose and combinational drug therapy. Until 25 years ago chemotherapy was applied mainly to leukemias and lymphomas in a continuous single agent method but now the other principles are being used with huge successes in chonocarcinoma Burkitts lymphoma, Wilm's tumour, acute lymphoblastic lymphoma and embryonal rhabdomyosarcoma.

Chemotherapy has the advantage that the drug enters most cells of the body, attaches to the intruding

Excerpt from an interview on Cancer with Dr. J.L.I. Odili

Chinedu Nwigwe and Anelechi Anyanwu

On Cause of Cancer. If anybody pinpoints the cause of cancer, that person will of course receive a Nobel Prize. and if we know the actual cause, naturally that will lead to development of specific treatment. By the term 'cause' here, I am referring to the pathological mechanisms by which normal cells transform to cells with malignant potentials. What we know are the factors or agents which do give rise to clinical cancer. We have chemical causes such as nicotine in cigarettes, aflatoxin, chemicals in food, industrial chemicals.... we have viruses such as HBV, EB virus, papilloma virus and herpes simplex virus. We have ionising radiation – from sunlight, diagnostic X–ray machines, nuclear fall out of atomic weapons and nuclear plants.

Mechanism: Exposure to these agents as well as co–existing factors in the individual such as diminished immune status, genetic status, hormonal imbalance, or pathological process such as liver cirrhosis, all lead to the causation of cancer in different individuals. These aetiologic factors most likely affect or interact with genes in normal cells to form oncognenes which stimulate the rapid, irregular uncontrolled growth of malignant cells.

Smoking and Nutrition in Relationship to Cancer: It is true that cigarrette smoking has been linked with cancers of the lung and cervix. If one does not smoke cigarrettes, ones chance of developing these cancers is decreased. In most Western Countries packets of cigarettes are labelled as health hazards. As for nutrition, if one does not have a balanced diet one can develop nutritional cirrhosis of liver, and cancer is one of the complication of cirrhosis. We have not ascertained how much carcinogens there are in the food we eat in the third world. Aflatoxin which is implicated in hepatoma was found in mouldy groundnuts. It has also been found in high concentrations in mouldy yam and other mouldy foods. This may contribute to the high incidence of hepatomas in developing countries. However, the high roughage content of our foods makes the transit time of food in the gut faster than that of Caucasians. This rapid transit time may help in the reduction of the incidence of cancer of the colon and rectum in this part of the world because the carcinogens do not have time to be absorbed. This is an advantage which should be maintained.

On Treatment and its Effectiveness: Effectiveness of

cancer cell and effects its elimination. However its degree of discrimination between cancerous and normal cells is low. Therefore, it can destroy the rapidly dividing normal cells leading to adverse effects such as depression of bone marrow activity, loss of hair on the head, reduced sperm count etc.

Hormonal treatment is based on the fact that some tissues growth is highly responsive to hormones (chemical substances produced in certain tissues which produce their effect on other tissues). A Scottish surgeon in 895 removed the tubes and ovaries of a 33 year–old breast cancer patient. This operation (oophorectomy) reduced the estrogen (hormone) which promotes breast growth and stimulated a rapid improvement in the woman's condition. In 1930, Higgins an American doctor treated cancer of the prostate by removing the testis – a process called orchidectomy. This reduced the amount of testosterone (male sex hormone) produced. Nowadays, synthetic hormones and antagonists are in vogue. An anti–estrogen called tamoxifen was discovered in the 1960s and is being widely used for management of breast cancer. Hormonal therapy is palliative and can produce remissions in about 80% of these cancers.

To arrest the guile of cancer, doctors now combine two or more of the approaches described above. Surgery and radiotherapy or surgery and chemotherapy and other suitable combinations are used to achieve maximum effect. Apart from the purely medical onslaught on cancer, hospitals, states and organisations are marshalling out different strategies to augment and complement the efforts of doctors.

At the UNTH, funds have been made available to a Joint Hospital Management Team whose aim it is to develop protocols for the treatment of various forms of cancer in this hospital. Thus a standard approach to treatment of each cancer is set out. This team would also facilitate purchases of cancer drugs so as to obviate the out–of–stock syndrome. A proper registration of neoplasias has also been instituted in this hospital.

The government, realising the importance of cancer in our society, has designated Ahmadu Bello University Teaching Hospital a centre of excellence for cancer radiotherapy and over twenty million Naira has been ear-marked for it. Also cancer patients are privileged to receive their drugs free, courtesy of the Federal Government. The major problem is that these drugs are not always available. Again cancer is not such a disease to allow its victim the convenience of queuing up for treatment with the better facilities at ABUTH. Consequently more facilities should be provided in various parts of the country to enhance easy access to good and prompt attention.

World Health Organisation (WHO) has also recognised cancer as a major public health burden and has taken positive steps aimed at unravelling and controlling this enigma. Apart from establishing a cancer Unit in its headquarters, International Agency for Cancer Research at Lyon France, it has initiated programmes aimed at stimulating exchange of information on cancer. The development of the WHO Blue–Books – the International Histological classification of Tumours, standardization of hospital–based cancer registries are additional efforts to hold the tide of this disease. WHO Regional Office for Africa located in Brazzaville is also toeing the line of the main body in promoting cancer control activities. They work along other organisations like the Nigerian Cancer Society.

Because the prospects of finding a quick solution to the cancer problem seem rather slight, prevention and early diagnosis of the condition which would save more

cancer treatment lies in early diagnosis. If cancer is diadiagnosed early, the patient has high chances of being successfully treated. I often talk of cancer control rather than treatment because cancer is such a difficult disease that you may believe you have treated a case, but 3–4 years later it may reappear.

Immunology and Cancer: Immunology was thought to be the end of cancer when it was discovered that tumour cells contain tumour specific antigens (TSA) not present in the normal cells of origin of the tumour. It was believed that cancer patients could be specifically immunised with their cancer cells. The products of the induced immune response would then specifically attack and destroy cancer cells only, leaving normal cells unaffected. The optimism was heightened when it was discovered that tumour specific antigens could be characterised with reference to the causative agent of the cancer. It was demonstrated that the TSA of chemically induced tumours were different from those of virus induced tumours, or tumours induced by physical agents. Detection of specific anti–tumour antibodies and sensitised T–cells was easily demonstrable in a variety of tumours. Cancer–bearing animals were found to have the ability to mount immune host defence mechanisms leading to spontaneous partial or total regression of their tumours. The above statements are easily shown to be true in the laboratory. Unfortunately these facts are not so clear cut in clinical practice. So far immunology has assisted the Clinician in understanding the pathogenesis of some tumours. It has been applied in demonstrating the possible causation of some tumours. However, its main application clinically has been in the treatment (immunotherapy) of cancer patients. The most commonly tried modes of immunotherapy are:

1. Use of patients own tumour cells (with the specific antigens) to immunise the patient against his tumour. This has been used with positive effect in breast cancers; melanomas and cancers of the head and neck.
2. Use of BCG, or other immuno stimulants to enhance the cancer patient's immunity (non–specific active immunotherapy) found to be effective to some degree in leukaemias, melanoma, leiomyosarcoma and adult renal tumours.
3. Adoptive immunotherapy in which T cells sensitised to a patient's tumour in vitro are re–infused into the patient.
   The results of this form of treatment are equivocal.
4. Use of preformed specific antibodies. This is not often used in man.

Active Immunotherapy is not often practised because of the fear that instead of inducing cytotoxic antibodies (in addition to sensitised T–lymphocytes) non–cytotoxic antibodies may cause tumour growth enhancement by coating cancer cells, protecting them from attack by T and killer cells which recognise them as normal.

lives and resources have been gaining favour. Dr. Odili asserts: "preventive measures against cancer lie mainly in awareness and avoidance. Awareness of what I personally call 'Warning Signals of Cancer', in other words symptoms that an individual may have which may lead the doctor to early diagnosis of cancer or precancerous condition. These 'Warning Signals' are irregular bleeding from any orifice—nose, mouth, arms, penis, an ulcer on the skin that would not heal, loss of voice which may be indication of cancer of larynx, change in bowel habit – constipation alternating with diarrhoea, a lump anywhere in the body...." This calls for intensive health education e.g. Breast–Self Examination.

Avoidance of cancer causing habits and agents is an even more pragmatic preventive measure than early diagnosis. This includes adoption of frugal diet, foregoing certain indulgences such as smoking, sunbathing and sexual promiscuity – this is important in the aetiology of cancer of cervix. The problem is that these actions compel people giving up pleasurable habits – an exercise that may have only limited success in the absence of acceptable substitutes.

However, more aggressive approaches could be adopted. They include strict legislation controlling carcinogenic chemicals, preservatives and artificial colours in foods. These substances include safrole used as a flavouring agent, diethyprocarbonate (DEPC) used in soft drinks, diethylstilbestrol, a sex hormone used in animal feeds. The Americans have highlighted the importance of legislation by inserting the 'Delaney Clause' in the 1958 Food Additives Amendment to the Federal Food, Drug and Cosmetic Act. we can implement this law here. Adequate legislative protection should also be given to high risk workers like miners, dye workers, soft–coal miners etc. Cancer Screening Programmes, though expensive, can be modified considering our environmental and socio–economic conditions and adopted even if it is only for the high risk population.

Recent advances in diagnostic and therapeutic facilities hold out a ray of hope. Development of antisera and vaccines, interleukins, and other immunological processes are all coming up. The use of ultrasonic probe in breaking down liver tumour cells because of its high water content leaving out the blood vessels and bile ducts which have low water content – has been started in the University of Philadelphia.

Cancer is really an enigma which has broken through cultural, racial and social barriers. It poses a big challenge to scientific endeavours and looks determined to be around for quite some time. However, with the combined efforts of governments, WHO, Cancer Societies and the increasing awareness of the populace, the march of cancer can be retarded drastically or even stopped. But the question is how soon?

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Pilot Survey of Public Opinion on Cancer in Enugu

— *Kenneth Omeche*

A survey aimed at finding out how well–informed the lay public are about cancer and its diagnosis, what opinion they held of the subject, and what has been the method of educating the public on cancer is presented.

Emphasis is placed on cancer of the breast and cervix as an index of public knowledge of cancer in general as these constitute the commonest female malignancies in Nigeria.[1]

Moreover the symptomatology of these cancers facilitates early detection and early treatment.

The survey reveals that a large segment of the population are unaware of the curability and preventability of cancer (particularly cancers of the breast and cervix).

It is also shown that the electronic media form the major source of information on cancer to the public

Introduction

The medical and scientific professions have continued to exert tremendous effort on research into the causes and cure of cancer. However, the lay public also has significant role to play in the control of cancer. But the public can only play this role if it is sufficiently informed about the disease. Early detection of cancer is the pivot on which complete cure revolves. Early detection of cancer of the cervix for instance, can be achieved by the use of papanicolaou smear (cervical cytology) as this can detect precancerous changes in the cell–lining of the cervix – cancer in situ (CIN 3). With this early detection and a combined early treatment, cancer of the cervix becomes a curable disease.[2]

Similarly, breast cancer when detected at stage I, II or early stage III (Manchester Classification), either by Breast Self–Examination (BSE), routine physical examination by a Clinician, or Mammography screening has a very good prognosis.[3]

Materials and Method

A total of 204 individuals – 141 females and 63 males participated in the study. The participants were drawn randomly from amongst traders, artisans, teachers and other civil servants in Enugu. The principal survey method was a self–report questionaire. Direct interviewing was however, done in majority of the cases not only for the sake of those who are not literate enough to fill the questionaire but also to ensure that respondents give correct interpretation to all the 16 questions in the questionaire.

Results

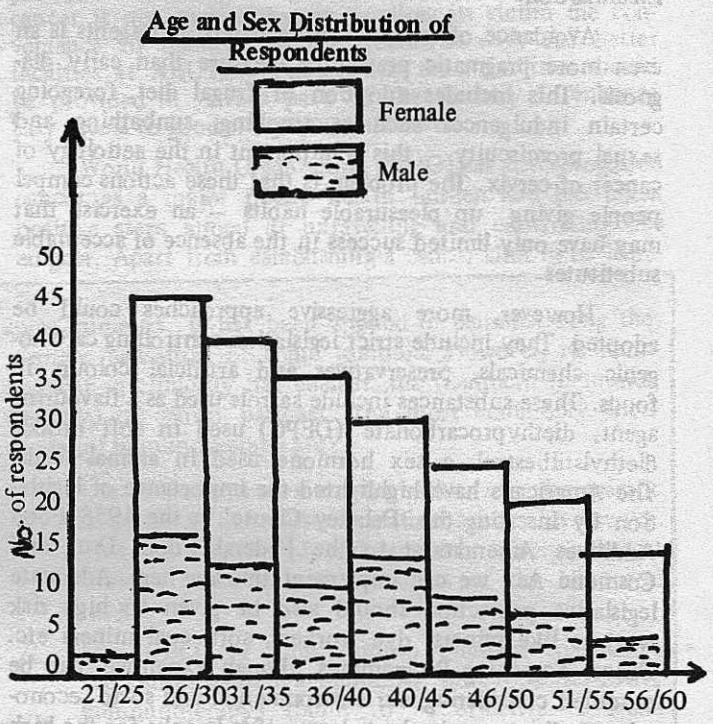
4 of the 204 questionaires were rejected for lack of merit, 200 were analysed.

(1) **Demographic Factors:** Questions were put to respondents on age, marital status, educational level attained and occupation.

KENNETH OMECHE, 5th year medical student, College of Medicine, UNEC.

(2) **Age:** The age and sex distribution of the survey population is shown below:

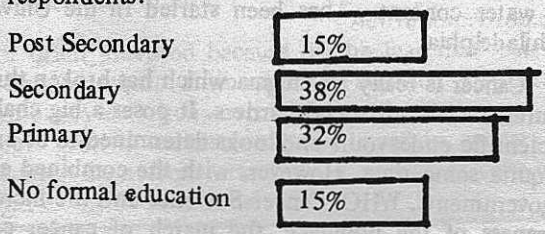
Fig. I



Five – Year age group

(3) **Marital Status:** 180 (90%) were married and 20 (10%) respondents were single.

(4) **Educational Level:** Figure II shows the level of education attained and percentage distribution of respondents.



(5) **Occupation.**

28 (14%) respondents were full housewives
54 (27%) market traders
48 (24%) were teachers
50 (25%) were civil servants and
20 (10%) artisans.

(6) **Questions on Cancer.** 190 (95%) respondents claim knowledge of cancer as a disease entity, 10 (5%) denied any knowledge of the disease. The table below shows the source of information on cancer.

Table I. Frequency distribution of survey population relative to information source.

Source of Information	Frequency
Radio/Television	171
Newspapers/Magazines	87
Hospital/Clinic	96
Friends/Relatives	76
Health books	33

When asked whether they knew anybody who suffered/is suffering from cancer, 96 (48%) answered in the affirmative. Of this number 86 (81%) answered 'no' to the question, was the patient cured of the cancer?

It is noted that cancer of the breast is the most widely known of all cancers among the lay public as is evidenced by their answer to the question, which part of the body was affected by the cancer?

(7) **Cure of Cancer:** Opinions varied on the curability of cancer.

Table II percentage distribution of respondents

Opinion on Cure of Cancer

	Women	Men
Cancer is curable	20%	21%
Incurable	51%	47%
Sometimes curable	25%	29%
Do not know	4%	3%
N (Female)	— 140	
N (Male)	— 60	

(8) **Causes of Cancer:** Various factors were advanced by respondents as the cause of cancer.

Table III Frequency distribution of public opinion on causes of cancer.

Causes	Frequency
Smoking	40
Alcohol	30
Putting money in bra	30
Hard drugs	20
Heredity	15
Micro–Organisms	10
Food additives	10
Cosmetics/dyes	9
Promiscuity	6
Spontaneous	4.

Those who cited putting money in bra related it specifically to Ca Breast.

(9) **Cancer Prevention:** On whether cancer can be prevented, 112 (59%) respondents believed cancer is not preventable, 64 said it can be prevented while 24 (13%) were undecided.

(10) **BSE & Pap Test:** The knowledge of women respondents about BSE and pap test was sought for. 83 (60%) women accepted having heard of BSE, 33 (24%) claimed to be practising BSE regularly. This figure is low when compared to a survey in U.S. where it was found that 67% of women practise BSE monthly (Gallup Organization. 1973)[4]. The figures in this survey also fall below that of Australian women where a survey showed that 84% of women are aware of BSE and 56% practise it on a regular basis (Hill D.J. et al 1975)[5].

When asked the source of information on BSE, 66 women cited Television/Radio, Newspapers, Magazines and Health books. 13(15%) claimed to have learnt of the method in the clinic while 5% learnt of it from friends/relations.

Only 40 (27%) of women knew about pap test and only 10(7%) go for regular pap test. These figures fall much less than that recorded for Canadian women where in a survey 76% of women have had pap test and in British Columbia where 88% of women have had pap test. (Philip A.J. et al 1975)[6].

74% of those aware of pap test got the knowledge in the clinic, 4% from books and magazines and 12% from Radio and Television.

Discussion

The survey establishes that a great deal of pessimism exists on the part of the lay public on the curability of cancer whether detected early of late. It is also found that health workers in clinics are not playing significant role in public education about cancer, as is shown by the few respondents who cited clinics as their source of information.

While cancer is a fatal disease if untreated or treated late the fact remains that early cancer is among the most treatable causes of death.

In this society, the greatest number of deaths from malignacies in women arise from cancers of the Cervix and Breast. Ignorance of the value and method of BSE and pap test among other factors results in delay in presentation at clinics until when symptoms become very discomforting and at which stage complete cure becomes difficult.

Educating the public therefore, on a disease whose remission is dependent on early detection and early treatment is imperative.

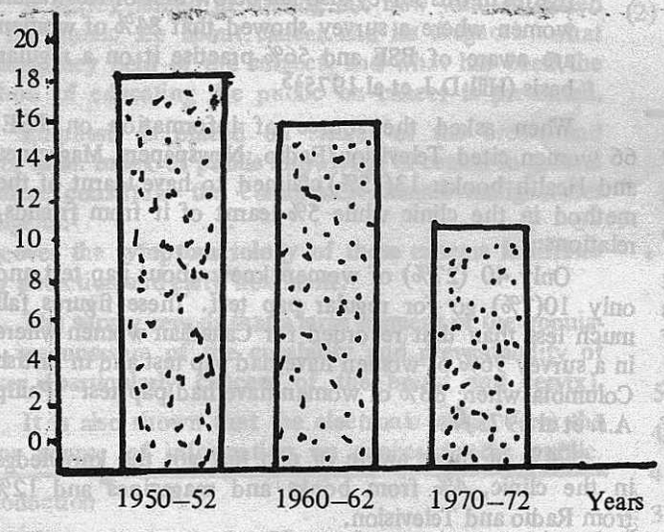
The role of BSE and pap test in reducing mortality from cancers of the breast and cervix respectively is shown by a Canadian survey. By questioning 1031 Breast Cancer patients as to their frequency of practising BSE and relating it to patients' delay, it was found that BSE is of great value in minimizing patients' delay in seeking medical attention.[7]

Table IV Relationship of Frequency of BSE practice to patients delay

Frequency	Mean delay
BSE Monthly	4.6 weeks
BSE Occasionally	7.1 weeks
BSE Never	9.4 weeks

In a related study in British Columbia where intensive

public education about cancer is carried out and preventive measures against cervical cancer in the form of regular papanicolau smear screening is done for a significant percentage of the female population over 20 years of age, the result has been a progressive decrease in the incidence and mortality from cancer of the cervix as is shown in the chart below.[8]



%Rate/100,000 women within ages 30 – 60 years.

Conclusion.

The survey has shown that there is a low–level of awareness of cancer among the public.

The implication of this state of awareness is that morbidity and mortality may continue to increase even where health facilities are increasingly made available as the cancer patient will still present late to clinic for anything life–saving to be done.

The solution to this problem lies in a vigorous public education campaign on cancer. The government has much role to play in this respect.

It is her responsibility to embark on a mass cancer screening programme for women. Free cancer screening centres should be set–up in government owned hospitals throughout the country in addition, the American cancer society's 1980 protocol for early detection of cancer in asymptomatic persons which recommended a monthly Breast–self examination for females over 20 years of age, an annual pap test for females over 20 years of age and an annual digital examination for both males and females over 40 years[9] should be adopted and widely disseminated to the public by both government and voluntary agencies.

Acknowledgement.

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VOLUNTARY BLOOD DONATION

Blood is a life–line.
Throw someone a life–line,
And prevent him from drowning.

Donate a pint of blood,
And prevent someone
From dying.

Help save someone's life.
That life may be yours.
Donate blood voluntarily,
Go to the blood bank of UNTH!

Why buy blood,
When you can donate yourself.

Blood donation is harmless.
I am going to donate voluntarily,
To save a life.
I think it is worth it, don't you?

Foreign Gene as a Marker in Cancer Therapy

The first experiment ever to insert genetically altered cells into human patient has been approved by a Review panel of the U.S. National Institute of Health (NIH). The recombinant DNA advisory committee of the NIH approved the experiment despite an earlier recommendation from its Gene therapy sub–committee that the experiment be shelved until more data about risks posed by the procedure is obtained.

Researchers hope eventually to use similar techniques – replacing missing or defective gene to cure some diseases caused by genetic mutation. The foreign gene in this experiment will simply serve as a marker helping researchers to monitor the progress of a treatment they developed for cancer. The treatment involves growing anti–cancer cells called tumour – infilterating Lymphocytes in a solution of interleukine–2 and re–injecting them into the patient.

A marker gene carried by a Retrovirus will be inserted-

PATHOLOGY

Neoderm theory of cancer

Joseph I.L. Odili

In this paper a theory is propounded that cancer is an evolutionary process which will eventually result in the development of a new germ layer – NEODERM or INTRADERM. The new germ layer will lead to alteration in the present anatomy and physiology of the human body, so that man will be better adapted to modern or "ultra modern" living. The simplistic presentation of this essay is deliberate.

Introduction

In defining cancer, emphasis is placed on the facts that cancer cells: a) grow in an irregular and uncontrolled manner, b) are of no benefit to the body, and c) if unchecked lead to the death of the patient. The reasons why cancer–causing agents trigger off such non–beneficial chain of reactions in the human body are not yet fully understood.

Over the decades, cancer–causing agents (carcinogens) have been identified. The list of experimentally demonstrated carcinogens is unending. However, they can be classified into chemical carcinogens, viruses, ionising radiation and physical agents. One wonders why such diverse substances such as nicotine, aflatoxin, viruses (such as herpes simplex, papilloma, hepatitis B viruses), radiation (from sunlight, x–ray machines, nuclear fission of atomic bombs) and inert physical agents, should give rise to similar cellular abnormalities resulting in cancer. There is thus, a common factor, – alteration in cell metabolism of a particular tissue or organ – resulting in wildly proliferating tumour cells.

Normal cells exposed to these noxious and toxic carcinogens would be expected to initiate self preserving defence reactions. Could it be that these wildly proliferating cancer cells might not mean harm at the onset, though later as a result of infiltration, obstruction, mechanical and metabolic effects, the uncontrollable cells prove harmful? Could it not be that cell proliferation to the stage we call cancer is initially a response on the part of the body to overcome an adverse situation? In other words, is uncontrolled cell proliferation (cancer) not an attempt by the body at survival, which is backfiring?

Some Basic Pathological Facts

Consider a few basic pathological facts:–

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1. HYPERPLASIA is basically a beneficial phenomenon and sometimes it is difficult to distinguish it histologically from neoplasia. The hyperplasia of a pregnant uterus is beneficial.

2. Tissues when irritated, assume more protective characteristics, for example (a) gall–bladder in the presence of gall stone, (b) inverted prolapsed uterus subjected to friction; (c) bronchial epithelium in a bronchiectatic lung – in all three instances the columnar epithelium becomes stratified squamous – METAPLASIA. This is also a beneficial phenomenon. Some would regard squamous metaplasia of bronchial epithelium due to irritation by cigarette smoke as the earliest stage in the development of bronchogenic carcinoma.

3. Some pathological conditions such as leukoplakia and polyposis coli are known to be precancerous.

4. Some benign neoplasms turn malignant eg. papilloma of the bladder.

5. Some benign neoplasms may be lethal from pressure or other effects eg. myoma of the uterus, thyroid adenoma, benign prostatic hyperplasia.

6. Slow growing malignant tumours are not as lethal as

7. Rapidly growing malignant tumours which soon metastasise, give rise to obstructive and pressure complications and are soon fatal.

The Cancer Spectrum

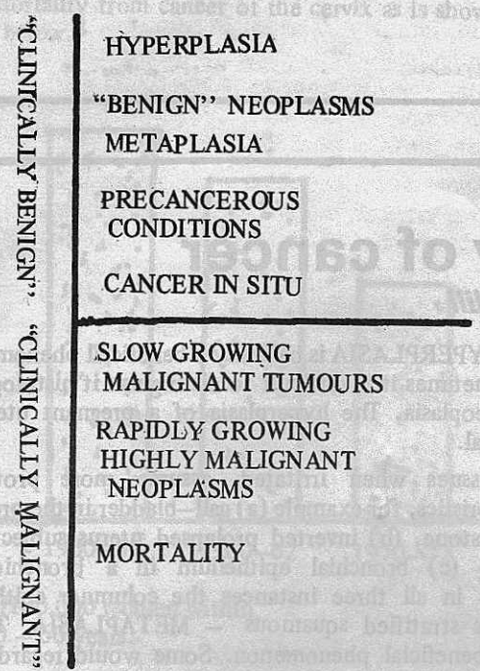
A consideration of the above seven points makes one inclined to think of "cancer" as a spectrum. At one end of the spectrum are hyperplasia and metaplasia, at the other end are rapidly proliferating highly malignant neoplasms. In between the two extremes lie benign neoplasms, precancerous conditions, cancer in–situ, and slow growing neoplasms of low malignancy.

The pathogenetic placing of individual lesions along this cancer spectrum depends on the nature, intensity and duration of exposure to the causative agent and the body's reaction and resistance to it.

Cancer – A Beneficial Process

Since the first components of this spectrum, viz. hyperplasia and metaplasia are established to be beneficial, could it not be that the cell proliferations which ultimately give rise to the other components of the spectrum are initially meant to be beneficial? This might well be so as supported by this fact. Chronic ulcers turn malignant, as in gastric ulcers and ulcerative colitis. At first the cells

DIAGRAM 1 – THE CANCER SPECTRUM



of the ulcer proliferate in an attempt to heal the ulcer, but the continued presence of the cause of the ulcer leads to continued overactivity of these proliferating cells, until when the stress reaches a critical point, the cells assume malignant characteristics. In other words, the cell proliferation called cancer may eventually turn out in future to be a beneficial process.

All Carcinogens as Stresses of Modern Living

Many carcinogens are products of modern development. Chemical carcinogens such as nicotine, aniline dyes, drugs, industrial chemicals and their toxic wastes, radiation from x–ray and nuclear explosions are results of modern development. Viral carcinogens may be results of genetic engineering and products of new viral strains for germ warfare. The depletion of the ozone layer is now exposing man to more cancer–causing ultra–violet radiation. No doubt there are many more carcinogens yet to be identified from such phenomena as atmospheric pollution, green–house effect and ecological changes. If one groups all carcinogens and calls them "STRESSES OF MODERN LIVING", could cancer not be regarded as the body's response to stresses of modern life?

It is well known that cancers of various organs have variable incidence depending on geographical area, social habits, racial groups and degree of modern development. Many aspects of modern living, be it the fast travel, the noise, the competition, the amenities, could be regarded as stresses to the body and one would imagine that among those stresses are carcinogens yet unrecognised as has cigarette smoke.

Evolution – Man's Future

If most aspects of modern life are carcinogenic stresses, then one can assume that the body, in its present anatomy and physiology, was not fashioned to stand these stresses of modern living. It means (if the last assumption is true) that with further advances in modern developments two courses are open about the fate of the human body and of mankind:–

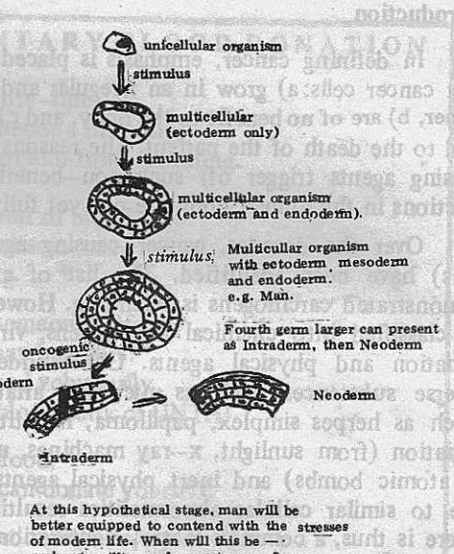
(a) either the basic anatomy and physiology of the organs will need adjusting to face these new stresses

or (b) man will make himself extinct by his advancements.

From the evidence of evolution, it is more likely that the first alternative will be the course of events i.e. that there will be some change in the body's anatomy and physiology.

A Fourth Germ Layer

How this change to a modern or ultra–modern body will be effected is anybody's guess. But one thinks that this is where cancer comes in; if the supposition that the aim of cell proliferation which results in malignant disease is a beneficial one, then one could suppose THAT CANCER WAS THE FIRST STEP TOWARDS EVOLUTIONARY MODERNISATION OF THE ANIMAL (HUMAN) BODY!



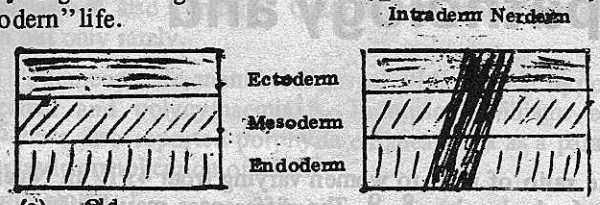
Consider the evolution of germinal epithelium for instance; the earliest most primitive animals had only one cell (amoeba), then came animals composed of ECTODERM only, then animals with ECTODERM AND ENDODERM, (hydra) and then those that had **Mesoderm** added (man). Each addition of a germinal epithelium resulted in a **higher** animal, more complex in anatomy and physiology, and better adapted to face more stresses.

In the evolution of monkey to man, there has been a change in the anatomy and physiology without addition of a new germ layer.

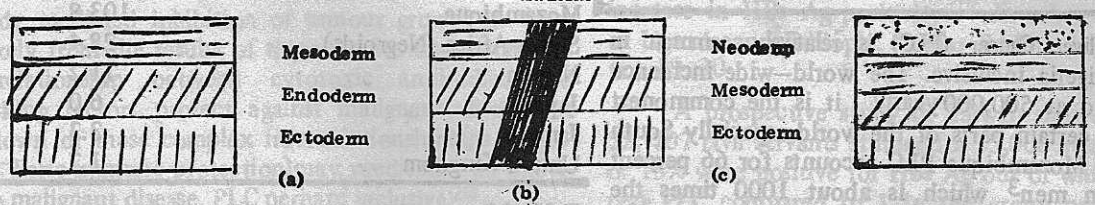
If the theory of evolution, that man evolved from lower animals is true, then there is no reason why man, as his body is constructed today, should be the ultimate goal of evolution, nor any reason why the third germ layer should be the limit in the evolution of germ layers.

One may therefore imagine that a time will come – (a million years time – who knows) – when man's body structure and working will be different from what it is

today. For this change, there will be addition of new growths, new tissues, – (neoplasia) – and remodelling. There may be even a new germ layer (a 4th one) which the author calls "**Neoderm**", or "**Intraderm**" (fig. 1). This new germ layer, one imagines, may form new organs or new tissues; "stress tissues" which would be incorporated into every organ making them able to withstand the stress of "modern" life.



It may be that this fourth germ layer has already started to evolve. Some tumours are believed to arise from embryological crests. These may be the very earliest forms of this new germ layer, not yet differentiated, but proliferating under stress to give rise to embryonic tissues from which they are arising thus, carcinoma if from ectoderm or endoderm, sarcoma if mesoderm, (see diagram 2).



Biological Evidence

This evolutionary theory or (neoderm) theory of cancer unfortunately cannot be proved overnight, nor for that matter experimentally in laboratories since man is the experimental animal, and the result of this 'natural' experiment will only be known to future generations.

However, experiments and/or clinical observations – establishing relationships between stresses of modern life and cancers of various organs will go some way towards supporting this theory – eg. establishing a relationship between noise and tumours of the auditory apparatus, or between types of food and cancers of the gastrointestinal tract.

Discussion

Over the years many diseases have initially been regarded as great scourges to humanity until medical science resolved the problems and cures for them were found.

Today, the disease Cancer is one of the scourges facing mankind. Scientists the world over are researching into many aspects of it – causation, pathological process, treatment and prevention. The disease is so dreaded that a diagnosis of cancer is often tantamount to a death sentence. In this paper, a light–hearted look at the disease is presented in a simplistic form to stimulate academic thoughts on the positive side of the disease: that Cancer is an evolutionary process which will ultimately be beneficial to mankind. At the moment the "new" Cancer cells proliferating under the stimulus of carcinogens have not intergrated into the present anatomy and physiology of the human body. Hence it is regarded as a disease.

To go into the pieces of evidence in favour or against the theory will require a much more in–depth medical, religious, biological, anthropological and evolutionary analysis.

These questions then come to mind. In which lowest mammals can cancer occur? What is the prevalence of cancer in apes? What are the anthropological findings about cancer in lower animal forms or the findings about the evolution of apes to man – the anatomical changes between the primitive man and the modern man?

Indeed religion may not agree with the theory of evolution. In the beginning, God created the world, the living beings, Adam and Eve in the garden of Eden. Against this, the Scientist believes in the "big bang" and the consequent formation of the solar system of which the earth is an outcome.

Even believers of evolution of a man have many theories to contend with. Is Darwin right or is Lamark right?

What are known and agreed by most are that in the evolution from single celled animals to planktons, to two germ cell layered animals such as hydra, to lowest mammalian forms with ectoderm, endoderm and mesoderm, and from the lowest mammalian forms to modern man,

1. There has been increased complexity in the anatomy, physiology, metabolism and in the ability to carry out sophisticated mental and physical activities.
2. Between animal forms with single, 2 germ layers and 3 germ layers are animal forms which are now extinct.
3. The manner of development of the germ layers and the higher animals is not known.

The theory proposed here is that cancer offers an answer to some of the questions posed here. The uncontrolled prolifieration of cells which we call cancer will eventually be beneficial, being the earliest formation of a fourth germ layer which will result in changes in the present day anatomy, histology, physiology, biochemistry of the ultra modern man, thus preventing him from dying as a result of exposure to the carcinogenic agents of man's development and thus ensuring man's future survival from otherwise inevitable extinction.

Primary liver cancer — a review of its epidemiology, pathology and prevention

— *Patrick I. Okolo (Jnr)*

In this review, the increasing and widespread incidence of Primary Liver Cancer (PLC), is highlighted. The disease seems to be the effect of the interaction between different genetic and environmental factors with immune breakdown as the final common pathway to pathogenesis.

The development of hepatitis B virus vaccine and its subsequent application coupled with a better understanding of the aetiopathogenesis of PLC would significantly reduce the incidence of the disease.

Primary liver Cancer (PLC) is relatively common in the tropics, Nigeria inclusive. The world–wide incidence being estimated at 500,000 yearly - it is the commonest malignancy in certain parts of the world especially South East Asia[2]. In Mozambique PLC accounts for 66 percent of tumours in men[3] which is about 1000 times the incidence in most of Europe. These high figures, which rightly assert the place of PLC as a "captain of the men of death" have interested the author of greater interest, is the increased understanding of PLC through intense research efforts leading to three important developments:

Full import of PLC has been realized by epidemiology.

A new awareness of the importance of environmental factors in the oncogenesis of liver cancer.

The prospects of the prevention of this scourge through recent developments in hepatitis B vaccine.

Distributions

There are geographical variations in the incidence of Primary Liver cell carcinoma (PLC). The majority of patients being found in the Orient, though Mozambique in South East Africa has the highest incidence[4]. It has been estimated that about 11,200 Nigerians out of an estimated population of 100 million develop PLC annually[5].

These differences in incidence may not be solely due to geographical factors since there are differences within subgroups in a heterogenous community; studies have also revealed that immigrants from a country of high incidence have a higher incidence of PLC than the local population but have a lower incidence than those resident at home[6]. It is also interesting to know that the converse is also true. Chinese born in singapore have a higher incidence of PLC than immigrant Chinese to Singapore[6]. It is only then logical to assume that cultural and socio–economic factors have also a role to play in the incidence of PLC. PLC occurs mostly in young males in their 20s and 30s, the ratio of men to women varying from 4: 1[7] in Nigeria to 6: 1 elsewhere[8, 9]. The differences may be due to a genetic susceptibility or to differences in exposure to carcinogens.

Table 1 (Triger D, 1987)

Variation according to location — Incidence of Primary liver cell cancer

Country	Incidence (Per 100,000)
Mozambique	103.8
South Africa (Negroids)	28.4
Nigeria	11.2
Japan	6.0
Jamaica	3.3
United Kingdom	1.7

Table 2*

Annual Incidence of hepatoma in subcommunities in different countries.

	Country	Males/100,000 population
(.)	South Africa	
–	Negroid	28.4
–	Indian	9.5
–	Caucasian	1.2
(.)	Hawaii	
–	Aborigines	15.2
–	Chinese	7.3
–	Japanese	6.7
–	Cancasians	4.3

* Source: Trigers Series, 1987

Pathology: The majority of these hepatic tumours, arise from hepatocytes and are adenocarcinomas[10]. There are, however, two major types, those arising from the liver cell and those from the billiary tract–cholangiocarcinomas.

Apart from PLC, other epithelial tumours of the liver include cholangiocellular carcinoma, bile duct cystadenoma, combined hepatocellular and undifferentiated types[11]. The classification of PLC is based solely on histopathological appearances, various subgroups have been described but variegated and mixed patterns are seen also. The major histological subtypes are: (i) Adenoid (ii) Giant cell (iii) Anaplastic (iv) Pseudo endothelial (v) Miscellaneous[12]. The essential feature of these is the resemblance to hepatocytes. The tumour cell exhibits features of malignancy interspersed with areas of necrosis and absence of Kupffer cells and macrophages the sinusoidal spaces are usually filled with haemorrhagic material and there is usually, an associated macronodulor cirrhosis.

A histological study of 144 post mortem livers from

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patients with PLC at the University College Hospital Ibadan showed 87 percent to be of adenoid and giant cell varieties, cholangiocarcinoma only accounted for 8 percent, the remainder was accounted for by other forms[13].

Metastasis is largely by lymphatic spread, however, haematogenous spread to hepatic veins with pulmonary metastasis is also common. Other visceral metastases are seen but only rarely.

Paraneoplastic manifestations of PLC include hypoglycemia and polycythaemia[14]. Thompson, Williams et al[15] have also reported porphyria cutanea tarda as a paraneoplastic complication of PLC.

Immunology

It has been long thought that the genesis of malignancy in an individual is related to a breakdown in the immune surveillance mechanism. PLC is no exception to these postulates. Studies on other malignancies – carcinomas of the breast, ovaries, testes, kidneys, and sarcomas, have demonstrated cytotoxicity and tumour cell colony inhibition by blood lymphocytes[16, 17].

Other studies,[18, 19] have also demonstrated humoral antibody mediated inhibition of tumour growth in vitro, it is likely from the results of these studies that a complex inter–relationship between cytotoxic antibodies and unblocking factors protect against malignant disease. A breakdown of these complex inter-relationships (as suggested by Earie immune protection) may predispose an individual to malignant disease, PLC perhaps inclusive[20]

The immunology of PLC has not been studied conclusively, but it is, however, logical to propose that the period between the onset of hepatitis, cirrhosis and PLC is the period during which the immune response is slowly overwhelmed. The fact that the continuance of chronic perenchymal liver disease is associated with a continuously high hepatitis B surface (Hbs Ag) antigenaemia despite high levels of specific antibody is a pointer to immune response defectiveness. Various reasons have been given for the defectiveness of the immune response; Savel et al[20] suggested that aflatoxins have immuno suppresive properties hence their role in the aetiology of PLC.

Edington and Giles[21] also thought that hereditary factors were important determinants of this defective immune response. These hereditary factors may be linked to histocompatibility antigens (HLA) and may help to explain racial/heredofamilial susceptibility to this disease. Further research on this may yield important information; further research is also desirable so that immunotherapy may be used more effectively by physicians in the treatment of these individuals with PLC.

Alphafetoprotein, a specific alphaglobulin of Embryonic origin is found to be elevated markedly in PLC and serves as a tumour marker for it. Alphafetoprotein (AFP) is thought to be produced in the cytoplasm of malignant liver cells and has been found by studies in Nigeria and elsewhere to be of diagnostic significance in PLC. Workers in Ibadan found high levels of AFP in the cytosol of malignant liver cells[22]. Serum levels diagnostic of PLC were found in 94 percent of papua New Guinean patients[23] and in Uganda, positivity ranged from 71–93 percent[24]. In advanced PLC, the level of alpha–fetoprotein is commonly in thousands (normal level : 1ng/ml); a value of 2000ng/ml is diagnostic of PLC[25].

It is pertinent to note that AFP is also elevated to a lesser extent in tumours of the gastrointestinal tract as well as teratocarcinomas i.e. of testes. Despite this, AFP is still useful both for screening and follow up of PLC.[26]

It has also been observed that vitamin B12 levels and vitamin B12 binding protein are elevated in PLC, as in chronic myeloid leukemia. Serum ferritin is also elevated in PLC patients.[27]

Aetiology

The aetiology of PLC is multifactorial, a brief review of important factors will be considered in this paper.

(1) Hepatitis B Virus

Recent studies have shown this virus to be of great importance in the aetiology of PLC, the evidence for this being derived from many sources viz:–

(a) Epidemiology

Case control studies have shown a close co–relation between HBs Ag, postnecrotic cirrhosis and PLC, this has been proved in both high and low prevalence areas. Studies in Nigeria comparing 100 patients with PLC with a control group of 100 patients showed that there was a five fold increase in HBs Ag positivity.[28] In other countries such as Uganda and Ethiopia, similar findings have been reported. [29, 30]

A prospective study in Taiwan showed that out of 22, 707 civil servants studied for 75,000 man hours, 3, 454 or 15% were positive for HBs Ag out of which, 40 developed PLC compared to 1 in the group negative for HBs Ag. This result is very significant and it establishes the role of hepatitis B virus (HBV) in the oncogenesis of PLC.[31]

(b) Virology

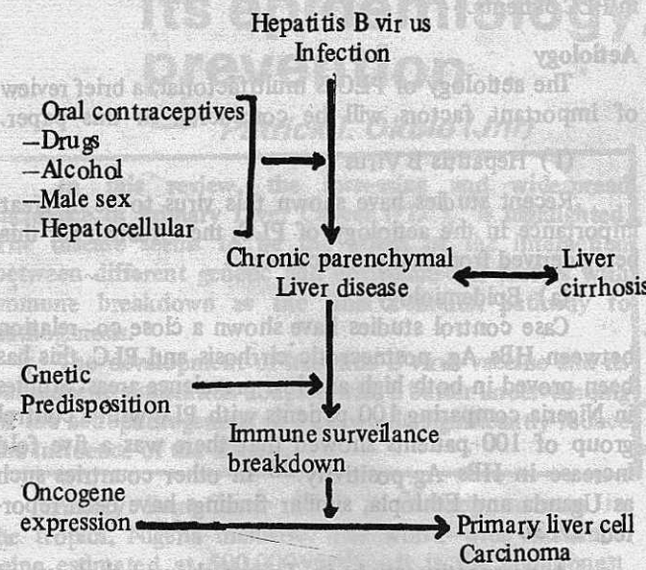
Recent studies have shown HBV to be a DNA virus which posesses its own DNA polymerase (a 42 DANE particle).[32] On first entering the cell the virus may replicate using its own polymerase and thus release viral particles. The circular DNA of the virus may become integrated into the host cell DNA; subsequently, a transcription and translation of host cell enzymes occurs probably resulting in malignant transformation, credence has been further lent to this observation by the detection of viro/DNA particles in the liver.[32] It has been proposed by the author that changes in the activity of liver cell enzymes may be responsible for the defectiveness of the immune surveillance mechanism. Other studies have already demonstrated this defective immune response.[37]

In spite of the strong evidence linking the HBV with PLC, it is unlikely to be the sole oncogenic[35, 36] agent as many HBs Ag negative PLC patients exists.

Other environmental agents implicated include alcohol, cirrhosis, oral contraceptives and male sex; these factors all seem to predispose to PLC because they are primers of chronic parenchymal liver disease.

Worthy of mention in the aetiology of PLC is the implication of certain hepatoxins in the oncogenesis of PLC. Aflatoxins are the most important group of these toxins, they are by–products of the action of the the action of the fungus Aspergillusflavus on mouldy groundnuts.[37] Lope[3] and crawford[38] in Uganda estimated that 16kg of groundnuts were required to reach the LD50 of a duckling. It is alarming to note the high concentration of aflatoxins found on Nigerian dining tables as highlighted by Nwokolo and Okonkwo.[39]

In summary PLC, seems to be the effect of the interaction between different genetic and environmental factors with immune breakdown being the final common pathology to the development of liver cancer. A possible scheme of events as adapted in fig. 1 would be:



(adopted from Triger's schema)

Any Hope For Prevention of PLC

Studies of the aetiopathogenesis of PLC are still going on with a view to giving added impetus for preventive measures working at the level of the HBV[40, 41]. Based on our present knowledge the development of the hepatitis B vaccine presents a ray of hope.

The vaccine is of two types, the initial type consists of a highly purified formalin, inactivated HBs Ag particle derived from the plasma of chronic antigen carriers. It is highly potent and it reduces the incidence in exposed individuals by 92%[42]. At the moment, antibody production to current vaccines lasts for about 5 years and therefore repeated vaccinations are necessary for significant impact to be made on the prevention of hepatitis B virus hepatitis. The use of the formalin inactivated vaccine is limited for large scale purposes because of its expense. This problem has, however, been solved by the development of a new vaccine using recombinant DNA technology. These vaccines are as immunogenic as serum derived vaccines. They are likely to open up the possibility of fascinating the world population against hepatitis B infection. Because they are cheap and supplies are not limited.

Assuming that current knowledge about the oncogenesis of PLC is correct, the development and subsequent use of HBV vaccine would have a very important effect on this disease. Vaccination programmes have already commenced in China and singapore and a task force on hepatitis B virus infection has been set up in Nigeria. The results of these laudable programmes are being awaited by a medical community anxious to see a reduction incidence of this disease that is at the moment, a "captain of the men of death".

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Acute leukaemia — An update

— *Godwin O. Obi*

The epidemiology, pathology and management of acute leukaemia is presented. Chloroma is noted as an important form of presentation of AML in Nigeria and other parts of Africa when compared to western countries, there is also a poor response to treatment.

The poor response to the treatment of acute leukaemia is associated mainly with the inadequacy of cytotoxic drugs, radiotherapy and supportive measures (such as blood components).

Leukemia is the term given to a group of disorders in which there is an aberration in the control of proliferation or maturation of haemopoeitic cells. The result is infiltration by leukemic cells of the tissues such as the spleen, liver, bone marrow and the lymph nodes. The accummulation of leukemic cells is usually associated with the appearance, in the peripheral blood, of primitive leucocytes. Acute leukemia is characterised by a large proportion of primitive or blast cells which morphologically may be assigned to one of the cell types – myeloblast, monoblast or lymphoblast. Sometimes however, the leukemic cells are so primitive that it is very difficult to assign the leukemia to a cell type. Clinically the acute leukemia progresses rapidly to death if untreated.

Epidemiology:

Leukemia appears to be seen less frequently in tropical countries than in western countries. This geographical difference has been confirmed by reports from East and West Africa. However, apart from this, it appears that a racial variation also exists for example the lowest frequency of leukemia has been recorded among the Chinese of Singapore.

Studies of the pattern of leukemia in Europe and North America show that between 1960 and 1970, the peak incidence of acute leukemia was found among children up to 4 years of age. Subsequently, the disease remained stable in adolescence and early adult life. After 50 years of age there was a steep rise in the incidence with increasing age. However, in tropical Africa as shown by reports from Nigeria, Ghana and East Africa, this pattern of occurrence is not found. There is an extreme rarity of acute leukemia below 4 years of age. By contrast there is a high incidence in the 10 – 29 year groups. Explanation of these differences between Caucasians and tropical Africa is as follows: In Africa, infections and malnutrition are common, and these may be a major factor in the loss of children in the very early years before the effect of leukemia could be manifest. Secondly, the high immunoglobin levels in neonates in Africa may be important in the protection of young children against infective agents which may cause leukemia. The delayed peak in acute leukemia in late childhood and adolescence coincides with the period when the influences are no longer important.

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Aetiology of Acute Leukemia

There are probably several factors that are responsible for the development of acute leukemia. It has been proposed that it is the interaction of the factors which initiate, in the susceptible individual, the clone of cells whose growth leads to acute leukemia. The leukemic change is initiated in the leucocyte, with the neoplastic features being retained in all descendants of that cell. It does follow that leukemic change must involve an alteration in genetic material, which is transmissible. Aetiologic or susceptibility factors must of necessity possess the potential for action on nucleic acid – the basis of biological information. Four classes of agents fulfill this requirement and have all been implicated in leukemogenesis:
(i) Radiation (ii) Drugs and Chemicals (iii) Genetic and Chromosomal factors (iv) Viruses.

i. Radiation: The most convincing evidence that ionising radiation can cause leukemia is derived from the following groups of individuals: patients with ankylosing spondylitis who were treated with X–Rays to the spine; patients with polycythaemia vera treated with X–Rays or radioactive phosphorus; survivors of the atomic bomb explosions over Nagasaki and Hiroshima in 1945, in which those within one kilometer of the blast had the highest incidence of leukemia; and children whose mothers had abdominal X–rays during pregnancy. Radiation acts by inducing chromosomal breaks and combinations. It also induces oncogenic virus reduplication in vitro.

ii. **Drugs and Chemicals.** Benzene has been known to cause leukemia for many years. In 1978, in Turkey, what may be described as an epidemic of leukemia occurred among leather workers who used benzene as a glue–solvent. Exposure to toluene has also been implicated in the causation of leukemia. Of the cytotoxic drugs, the alkylating agents have been implicated. Such drugs are often associated with immunosuppression and chromosomal breaks. And in experimental animals, tumour growth enhancement can be found perhaps as a result of reduction of immune resistance to neoplastic cells. Chloramphenicol is also mentioned, and a few patients who had this drug eventually had leukemia. However causal relationship seems to be weaker than in alkylating agents.

iii. **Genetic and Chromosomal Factors.** It has been suggested that genetic and chromosomal factors could play a part in the causation of leukemia.

The following are the examples:

(a) Identical twin of a child with leukemia has a 20 to 25% risk of developing leukemia within one year of the diagnosis in the sibling. The chance in a non–identical twin is much less.

(b) Hereditary immunodeficiency diseases such as hereditary sex linked immunodeficiency disease and ataxia telangiectasia have a high risk of developing leukemia.

(c) In Down's syndrome (Trisomy – 21) it has been observed that there is a twenty fold risk of developing acute leukemia than in normal children. Similar observations have been made in the case of Fanconi's anaemia – another inheritable disorder characterised by chromosomal aberrations.

iv. **Viruses.** In animal species there is direct evidence that RNA viruses or retroviruses and some DNA viruses (herpes type) cause leukemia. Well known examples are the RNA virus of Rous sarcoma of fowl and the murine leukemia virus described by Gross. The part played by these viruses has led to the search for definite evidence in human leukemia. For example, Type C RNA virus particules have been demonstrated in some human leukemic cells using electron microscopy. Reverse transcriptase has been found in some acute myeloblastic leukemia cells. This enzyme allows viruses to form a DNA copy of its RNA sequences.

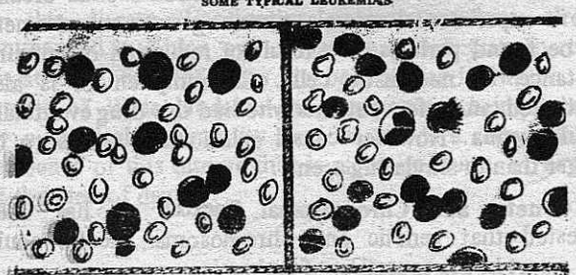
Mechanism of leukemogenesis by retroviruses

An important landmark in the study of the effect of viruses in causation of leukemia, was made in the early nineteen eighties when actual tumour transforming gene (oncogene) was identified in the viral genome. This oncogen (v – onc gene) appears to develop through a recombination process of a given retrovirus with the DNA of the host cell. Equally important discovery is that normal DNA contains a family of genes (cellular oncogenes or c – onc gene) thought to regulate normal cell growth and development. The c–onc represents the cellular analogue of the retroviral transforming gene, v–onc.

It is proposed that one of the steps in the oncogenic process is the integration of the viral sequence close to the cellular oncogen. This insertion of the viral sequence induces transcriptional activation of the contiguous cellular onc–gene. The cellular onc–gene then proceeds to regulate the aberrent cell proliferation or differentiation.

In Burkitt's lymphoma a different mechanism probably occurs. The cellular onc–gene, myc, has been implicated in the aetiology and is located on chromosome 8. In Burkitt's lymphoma there is an 8 to 14 translocation, and this event brings the myc gene close to the immunoglobulin μ heavy chain gene which is located on chromosome 14. The result of this is the activation of B–cell tumor formation under the control of the immunoglobulin gene.

SOME TYPICAL LEUKEMIAS



ACUTE LYMPHOBLASTIC LEUKEMIA (Predominantly lymphoblasts) *Peripheral* Blood smear

CHRONIC LYMPHOBLASTIC LEUKEMIA *Peripheral* Blood Smear

Classification of Leukemias

Morphological characteristics have for some time been important in the classification of Acute Leukemia. Other laboratory procedures such as cytochemical, immunologic, and cytogenetic are complementary. More recently the addition of monoclonal antibody techniques is helping to achieve more precision and consistency in the grouping of the acute leukemias. The morphological classification is that proposed by the French, American and British (FAB) Co–operative Group. The original proposals included immunologic markers and electron microscopy, but depended mainly on the traditional Romanowsky stains such as the Leishman stain of peripheral blood and bone marrow, with addition of cytochemical Sudan Black and non–specific esterases. The acute myeloblastic leukemias are M1 to M3, M1 showing minimum evidence of granulocytic differentiation, (Table 1). Moderate granulocytic differentiation occurs with M2. M3 represents the hypergranular acute promyelocytic leukemias, the cells containing many red granules. A rare microgranular form also occurs. M4 and M5 are the monocytic leukemias in M4 both granulocytic and monocytic differentiation are present. M5 represents the pure monocytic leukemia. Erythroleukemia or Di Guglielmo's disease is designated M6; its main features are numerous erythroid precursors in peripheral blood and marrow and also myeloblasts. In Acute lymphoblastic leukemia (ALL) three subdivisions are recognised, (Table 1). The usual morphologic criteria also operate, but immunologic features are also taken into account. In L1 the cells are small, uniform, with scanty cytoplasm. L2 cells are pleomorphic, larger and with more cytoplasm and nucleoli. L3 are Burkitt type, with vacuolated basophilic cytoplasm. This type is most probably the leukemic expression of Burkitt's lymphoma, since the lympoblasts resemble Burkitt's lymphoma cells. Immunologically, the L1 type tends to have the common – ALL antigen, while the L2 appears more to be T–ALL or null – ALL. L3 is the most distinctive subdivision of ALL correlating well with B–cell properties, especially the surface immunoglobulin.

CLASSIFICATION OF ACUTE LEUKEMIA

TABLE 1

General Term	FAB	Morphology	Tests	Type Name
ACUTE MYELOBLASTIC LEUKEMIA	M1	Minimum evidence of granulocytic differentiation	Peroxidase, Sudan black	Myeloblastic
	M2	Moderate granulocytic differentiation	Peroxidase, Sudan black	Myelocytic
	M3	Hyper–or micro-granular promyelocytes		Promyelocytic
	M4	Granulocytic and Monocytic differentiation	Lysozyme	Myelomonocytic
	M5	Monoblasts and monocytes	Lysozyme	Monocytic
	M6	Erythroid precursors	PAS; erythro-blasts	Erythroleukemia

CLASSIFICATION OF ACUTE LEUKEMIA

TABLE 2

General Term	FAB	Morphology	Tests	Type Name
ACUTE	L1	Small, Uniform with Scanty cytoplasm	C–ALL antigen TdT PAS	Common All
LYMPHO–BLASTIC	L2	Pleomorphic, larger, more cytoplasm, nucleoli		T–ALL Null ALL
LEUKEMIA	L3	Vacuolated basophilic cytoplasm		B–ALL

Variants of Acute Leukemia.

1. The blast crisis of Chronic granulocytic Leukemia: This is the usual terminal phase of chronic granulocytic leukemia, when there is an increase in blasts in blood and marrow. Patients with blast crisis have an unsatisfactory response to drugs used in the treatment of acute myeloblastic leukemia.

2. Secondary Acute leukemia: This is the type which results from prolonged management of neoplasia with cytotoxic drugs particularly alkylating agents. This has been recorded following treatment of multiple myeloma with melphalan and Hodgkins disease with nitrogen mustard. Secondary leukemia has appeared as M1, M4 and M6, often preceded by sideroblastic anaemia or marrow aplasia.

3. Rarer variants of Acute leukemia. These include megakaryoblastic leukemia and plasma cell leukemia. In the first type, the cell is atypical, often small megakaryocytes. Some authors prefer to include it as M7 subgroup in the classification of Acute myeloblastic leukemia. The other, plasma cell leukemia, resembles multiple myeloma except that it has excess of plasma cells in the peripheral blood.

Management of Acute Leukemia.

The management of acute leukemia is divisible into (a) specific drug therapy (b) Supportive measures (c) others

(1) Acute lymphoblastic leukemia: (ALL)

This type of leukemia is common among children, and is much more responsive to treatment than the Acute myeloblastic form. Infact in centres in which all modalities of management are available, good response has been obtained in a high proportion of cases. The aim here is initially to induce a remission (clinically and haematologically). The best drug combination, and which has stood the test of time, is Vincristine and Prednisolone. A good remission induction is then followed by a phase known as the consolidation phase which may include such drugs as asparaginase and daunorubicin. These consolidation protocols are more likely to produce longer remissions.

Supportive therapy: includes the use of red cells, leucocytes or platelet concentrates to replace any lacking blood components. Except for red cell concentrates which can be prepared by simple sedimentation for lack of a refrigerated centrifuge, leucocyte and platelet concentrates, require the use of sophisticated equipment. The successful management of infection requires the use of appropriate broad spectrum chemotherapy to cover such organisms as gram negative, anaerobic and fungal organisms which often complicate this condition. Other measures for ALL include prophylaxis against development of overt central nervous system (CNS) leukemia, both in children and adults. This may be effected either by CNS irradiation or intrathecal methotrexate.

(2) Acute myeloblastic leukemia (AML). All varieties of acute myeloblastic leukemia including erythroleukemia may be managed in the same way. Generally the prospects for successful outcome in management are much less, and the most optimistic remission rates in this group of leukemia have ranged between 50% and 60%. And only a minority of patients survive for five years. Whatever advance has been made in the induction of remission in AML rests on the newer cytotoxic drugs – cytosine arabinoside and daunorubicin.

The current strategy for induction of remission is to give a patient a multiple drug regime continuously or intermittently long enough to destroy the leukemic cells in the marrow. The most successful drug combinations include Daunorubicin or its analogue doxorubicin, cytosine arabinoside with or without thioguanine. Other but less effective combinations include cytosine arabinoside and thioguanine, cytosine arabinoside plus cyclophosphamide. Some authors have added vincristine and prednisolone to these regimens. However, remission maintenance has not been as successful in AML as in ALL.

Supportive measures: Supportive measures are aimed at the prevention of bleeding, with platelets, or the treatment of infection with granulocyte infusions. The use of appropriate antibiotics for infection assumes a greater significance in AML than in ALL. Protective isolation ensures a consistent level of remission by avoiding epidemics of cross–infection.

Other measures are adjuvant and are directed at complementing the chemotherapeutic and supportive measures. They consist of (a) immunotherapy and (b) marrow transplantation.

Efforts to demonstrate leukemia specific antigens have not been successful; claims of immunotherapy in leukemia are not borne out by results. However some cases of AML have been reported to have benefited from immunotherapy using BCG plus blasts or methanol extracted residue of BCG. Marrow transplantation: Of all recent approaches to management of leukemia, marrow transplantation has proved the most successful, particularly in young patients with closely matched donors.

Certain features in our environment which contrast with the general pattern of management of acute leukemias in Western countries need be mentioned here. Chloromas have consistently been an important form of presentation of AML. Chloroma has been reported in other parts of Africa. Another important aspect is the poor response to treatment of the acute leukemias in comparison with developed countries. The lack of adequate cytotoxic drugs and the absence of radiotherapy and supportive measures such as blood components stand out quite clearly. With improvement in these modalities of management, better response and prognosis will be expected.

Suggested Further Reading

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MEDICINE

Current concepts in cancer therapy

— Chike M. Nzerue

The Introduction of interferons and monoclonal antibodies represent major advances in cancer therapy. Interferons (IFNS) potentiate the activity of body cells such as natural killer cells, which maintain immunosurveillance against tumour growth; they also exert anti–viral effects against oncogenic viruses. Monoclonal antibodies (MoAbs) are used to target and precisely deliver cytotoxic or radio–nuclide drugs on tumours. These two developments are significant and epoch–making because they would reduce the effects of chemotherapy and radiotherapy on normal body cells while amplifying the destruction of cancer cells.

Introduction

Cancer of different body organs remains a world–wide scourge. In the United States alone, according to the National Cancer Institute, about 785,000 new cases of cancer are diagnosed yearly.[1]

In the Nigerian environment, statistics are hard to come by but workers such as Solanke[2] believe the incidence is equally high. This high incidence underlines the need for new and more effective forms of prevention and therapy. Modern cancer treatment has evolved almost exclusively during the twentieth century[3]. Before 1900 few cancer patients ever hoped for cure.

Important milestones in the evolution of cancer therapy include the introduction of radical mastectomy (for breat cancer) by Walsted, the discovery of X–rays by Roentgen and the introduction of cytotoxic drugs by pioneers such as Huggins, Farber and Rhoads.

With time, it became clear that cancer was multi–faceted and crab–like in both it's response to agents used in treating it and the potential for its definitive cure. For some cancers, it would be necessary to combine surgery, chemotherapy, radiotherapy and immunotherapy in varying proportions.

Also since with cancer, cure was not always possible, relief of symptoms would sometimes be the goal of therapy.

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Two new hopeful developments which may revolutionise cancer therapy include immuno-therapy, using interferons and monoclonal antibodies.

A. Interferons and Cancer

Interferons are biological substances that exert wide spectrum antiviral activity in animal cells, and also possess other biological properties one of which is tumoricidal (cancer–killing).

Discovery of this important group of substances is credited to Alick Isaacs and Jean Lindenmann (1957) who noticed from experiment, that infection with one type of virus seemed to protect the host from infection by another virus by a putative mechanism of interference.[4]

Interferons are mainly glycoproteins of which several types have been described in several species – Human interferons fall into 3 basic types; Interferon–alpha (IFN–α), Interferon–beta (IFN–β) Interferon – gamma (IFN–γ). IFN – alpha is the predominant type produced by stimulating leucocytes with virus. IFN–beta is produced by fibroblasts in culture while IFN–gamma is produced only by T. lymphocytes.

Production of interferons and mechanism of action against tumours.

Production of any of the above interferons is initiated by the presence of substances called interferon inducers of which the following groups are known.

I. Animal viruses active or inactivated.
II. Bacteria or bacterial products.
III. Polynucleotides, antigens, mitogens and anionic polymers, mycoplasma, Rickettsia and chlamydiae.

The inducer acts by depressing the interferon gene thought to be on chromosome number9. This leads to transcription of interferon messenger – RNA (ImRNA). ImRNA undergoes translation, post transcriptional processing and it is then secreted into extra – cellular fluid (E.C.F.).[5]

The anti–cancer effects of interferons derives from

the actions of interferons on the immune system, and on cell growth and differentiation. At least three effector cells are thought to be involved: B lymphocytes, T – lymphocytes and macrophages. The so called non B non T lymphocytes may also be involved.

T – lymphocytes when activated can destroy antigens including tumour associated antigens by release of active substances called lymphokines. Gamma interferon has been discovered to be a potent lymphokine. The cell killing activity of groups of non B, non T – lymphocytes called natural killers cells (NK cells) is increased in the presence of interferon. NK cells represent the body's surveillance mechanism against tumour growth.

All macrophage functions are stimulated. Suggesting that interferons are macrophage activating factors. Interferons inhibit growth of cells, especially actively dividing cells – i.e. tumour cells.

The anti–cancer effects of IFNs may also be due to their antiviral effects.

Clinical Applications.

Today, some centers are treating a number of human cancers with interferons. Hairy cell leukaemia is now being treated with IFN – alpha (wellferon) prepared by wellcome laboratories and this treatment is highly effective.[6]

Other Human tumours in which interferon therapy is being tried[7] include:

Osteogenic Sarcoma
Multiple myeloma
Hodgkin's disease
Acute lymphocytic leukaemia
Breast Cancer
Malignant melonoma
Nasopharyngeal cancer.

For us in Nigeria, where hepatoma is fast becoming a scourge, it is interesting to note that some workers are now giving a combination of IFNs and antiviral drug, Ara – A, in patients with chronic Hepatitis B virus infection[8] (which is known to progress to Hepatoma). Wide spread clinical trials of this regimen are required in Nigeria, as well as a hepatitis B virus immunization programme aimed at reducing the incidence of this viral infection which is known to be the major cause of hepatocellular cancer in our environment.

Problems/Side effects of Interferon Therapy:

Fever, chills, headache, malaise, bone–marrow suppression can all occur.

In the main, use of interferons is limited by high cost of production and low availability. With recombinant DNA technology, increasing qualities are being produced.

B. Monoclonal Antibodies in Cancer Therapy.

Monoclonal antibodies (MoAb) are immunoglobulins produced by one group or clone of lymphocytes against an antigen.

The discovery of these MoAb owes a lot to research in multiple myeloma, a disease in which serum protein electrophoresis gives a discrete band:– suggesting that the lymphocytes or plasma cells involved secrete specific antibodies and are thus likely to be single or monoclonal in origin.

Monoclonal antibodies are now used to sharpen the aim of the cancer therapist.[10] The principle underlying the use of MoAb in cancer therapy is the fact that cancers have antigens which are preferentially or inappropriately expressed on malignant cells. It is with these antigens or tumour secretory products such as carcino–embryonic antigen (CEA) that MoAb react.

MoAb are used in 3 ways in cancer therapy.

Firstly, the unmodified MoAb can be used to activate host defence mechanisms in the treatment of lymphoma and solid tumours. In one such study involving eleven patients, one has remained in remission for forty–two months while five others had objective remissions within a shorter interval.[11]

Secondly, MoAb can be tagged to cytotoxic drugs, so that on getting to the tumour site the MoAb binds to the tumour antigen and releases the drug. This has the effect of localising the cytotoxic drugs on the tumour and reduces systemic toxicity. MoAb–conjugates with conventional cytotoxic drugs such as methotrexate, adriamycin and vindesine have been prepared and have been experimentally found to be effective against human tumour grafts (xenografts) in immuno – compromised rats.[12,13]

Finally, MoAb can be used to target radionuclide therapy on the tumour. One study has reported treatment of fifteen patients with cancer of the ovary with intraperitoneal injection of the 131 I labelled MoAb. Toxicity, was noted at high doses though symptoms improved in most patients and complete remissions were achieved in those with stage 3 or less clinically advanced disease.[14] Intrahepatic arterial infusion of 131 I – labelled MoAb reacting with CEA is being currently investigated for hepatic secondaries from cancer of the colon. A similar study is being carried out on Neuroblastoma.[15]

Problems with MoAb in Cancer Therapy

Most studies have been carried out using MoAb to single tumour antigens, whereas there is strong evidence that a large proportion of tumours are heterologous in their antigen expression. This means that a cocktail of MoAbs of different specificities will be required to increase frequency of binding to tumour cells.

It is also possible that MoAb can cross – react with normal tissues to produce toxicity with drug conjugates but this is difficult to assess since lack of expression of human antigens on animal species means there is no experimental model to assess this. But it is known that anti – CEA MoAb also reacts with granulocytes when used to localise colorectal cancer. They also cause fever, rigors, emesis and a 40–90% drop in white cell count. The addition of interferons and MoAb to the cancer therapist's armamentorium would certainly extend the frontiers of cancer therapy.

Conclusion

This work shows that there is a great thrust to find new modern methods of treatment for the devastating and fatal disease cancer.

The addition of interferons and MoAb to the cancer therapists armamentorium would certainly extend the frontiers of cancer therapy.

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Cancer prevention — A special review

— Francis O. Chukwuani, Gabriel O. Eze and Obiekezie Agu

Current medical journals are reviewed and the various ways in which one's occupation, nutritional habits, familial tendencies, social behaviour, accidental and iatrogenic factors, can lead to cancer, are outlined.

A systematic analysis of preventive measures for each risk group shows that improved epidemiological studies and routine medical examination are of paramount importance in arresting the rising incidence of cancer especially in developing countries.

Introduction

Cancer, an intractable disease of all times, is second in mortality rate only to coronary artery disease in the western world[1]. In Nigeria and West African Sub—regions, the rising incidence of cancer mortality is compounded by the lack of facilities for the management of diagnosed cases. Thus, emphasis on cancer prevention is an important basis for successful medical intervention.

Cancer prevention refers to all that is known in relation to causation of neoplastic diseases and the avoidance of exposure to causative factors[2]. It also includes the recognition and treatment, where possible, of precancerous states, but does not include the early diagnosis of the established disease.

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People can be predisposed to cancer in various ways — by how they are from birth (congenital factors), how they live (habits) and where they live and work (psychophysical environment). Thus, the identification of those aspects of people's way of living as well as environmental agents or circumstances associated with the risk of cancer (for the yet unborn or for the living adults) could offer hope for efficient and successful prevention.

Method

This work reviews about twenty medical jorunals in our medical school library with reference to carcinogenesis and prevention mainly within the period, 1980 — 1988.

The findings are articulated and used to delineate six major risk factors: Occupational, Nutritional, Congenital or Familial, Accidental, Iatrogenic and Behavioural.

Preventive measures are outlined for the groups at risk based on our opinion on which aspects of the principle of cancer prevention are feasible for developing countries.

Findings

Tables, 1 a, b, c, d, e and f illustrate the integration of the findings from the reviewed journals with respect to risk factors (or groups) for certain cancers, and their respective scientific evidence. Possible mechanism of the carcinogenesis is incorporated in each case and some illustrated to indicate the site(s) of preventive intervention.

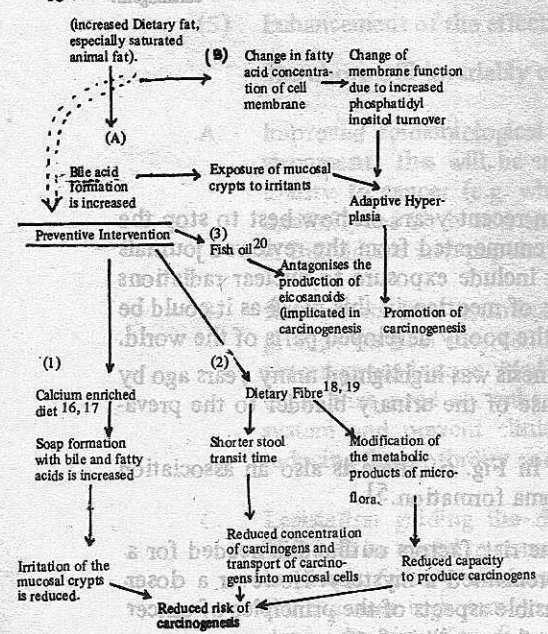
TABLE 1(a) – OCCUPATIONAL RISK FACTORS

	Occupation or Individuals at risk	Associated Cancer(s)	Scientific Evidence
1.	Painters, plastic factory workers, Dye/Rubber/Coal gas manufacturers – exposed to organic solvents such as benzene, toluene, xylene, trichloroethylene and styrene.	Leukaemia Lymphoma	Epidemiology[3] and Human Case Studies[4] Mechanism – metabolities could trigger off malignant transformation of target bone marrow cells.
2.	Abattoir workers exposed to bovine leukaemia virus and some animal carcinogens (while treating animal skins)	Soft tissue sarcoma, non-hodgkins-lymphoma, Acute Myeloid leukaemia.	Epidemiology[5] Mechanism: the oncogenic virus or carcinogens affect the genome of target cells (sequence of events is unknown).
3.	Wood workers exposed to wood dust (e.g. carpenters, cabinet workers, sawyers).	Nasal cancer	Epidemiology[6] Mechanism. abnormal irritation of the nasal mucosa leading to metaplasia.
4.	Children of male electronic workers exposed to electromagnetic waves	Neuroblastoma	Human Case Studies[7] Mechanism: the waves probably cause alteration of mitotic process in the father's rapidly dividing cells (e.g. spermatozoa).

TABLE 1(b) – NUTRITIONAL RISK FACTORS

	Risk Factors	Associated Cancer(s)	Scientific Evidence
1.	High intake of saturated fat of animal origin e.g. cheese, and other diary products.	Cancer of the colon and breast	Epidemiology and Animal Experiments.[8] Mechanism: See Fig. 1.
2.	Iodine deficiency in diet.	Thyroid cancer (especially folicular and anaplastic types)	Epidemiology[9] Mechanism. uncontrolled adaptive hyperplasia of the thyroid gland.
3.	Inappropriate cooking methods e.g. overfrying and excessive broiling of meat and fish, smoking and salting of food; nitrate curing of food.	Oesophageal and Gastric cancers	Experimental carcinogenesis in man and rodents.[10] Epidemiology.[11, 12] Mechanism. See Fig. 2.
4.	Heavy alcohol consumption.	Breast cancer	Epidemiology[13, 14] Mechanism: alcohol increases the transport of some carcinogens to target cells.
5.	Consumption of inappropriately stored food e.g. damp – hot (warm) stored wheat, rice and corn contaminated with Aflatoxin	Liver Cancer	Experimental carcinogenesis and Human case studies[15] Mechanism: See Fig. 3

Fig. 1 (A and B represent the two possible pathways of carcinogenesis by dietary fat).



* Risk of adaptive hyperplasia is higher following jejuno – ileal bypass, subtotal enterectomy, duodenogastric reflux of bile, colonic anastomoses (suture line carcinoma) and ingestion of bile acids. Manouvres that causes colonic hypoplasia (e.g. Colostomy) could also be useful to some risk groups.[21]

Fig. 2 (Mechanism of Oesophageal and Gastric Carcinogenesis) by inappropriate cooking methods)

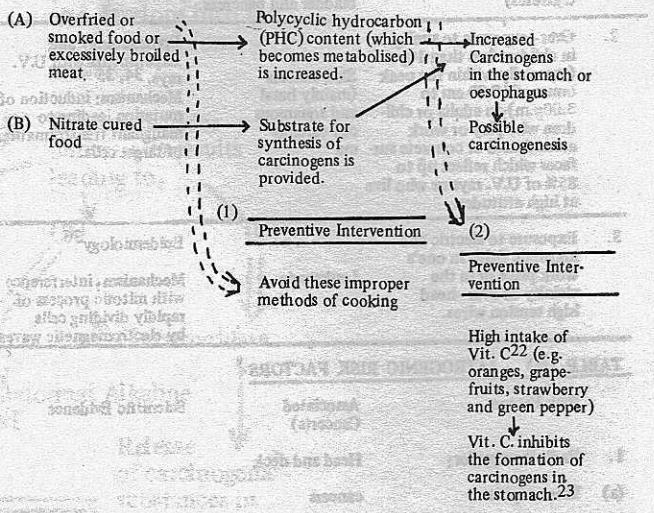
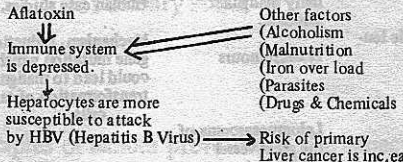


Fig. 3 (Aflatoxin and the risk of Primary Liver Cancer)



Preventive Intervention

- Proper storage of foodstuffs
- Inspection of susceptible foodstuffs to ensure that the level of aflatoxin does not exceed 20ppb[24] (especially in places where HBV infection is endemic).

TABLE 1(c) – CONGENITAL/HEREDITARY RISK FACTORS

	Risk Factors	Associated Cancer(s)	Scientific Evidence
1.	Down's syndrome (21 – Trisomy)	Megakaryoblastic leukaemia	Human case study. [25, 26] Mechanism. Abnormal chromosome 21 is associated with instability in the control of marrow proliferation.
2.	Sickle Cell Trait or sickle thalasaemia (especially when patients have a history of alcohol abuse).	Malignant Fibrous Histiocytoma (MFH)	Epidemiology. 27 Mechanism. Associated thrombotic episode could lead to increased risk of bone infarction which has been associated with MFH.
3.	Undescended Testes (especially if corrected very late in life)	Cancer of the Testes	Epidemiology and Human case studies. 28 Mechanism. High environmental temperature lead to retarded development, irreversible destructive changes and possible transformational changes in the testes.
4.	Exposure during gestation to maternal or exogenous estrogen	Cancer of the Testes	Epidemiology.[29] Mechanism. Unknown
5.	Family History of Breast cancer	Breast cancer	Epidemiology. [30] Mechanism. Unknown
6.	Klinfelter's syndrome	Extragonadal cerebral germinoma	Epidemiology.[31] Mechanism. Unknown

TABLE 1(d) – ACCIDENTAL RISK FACTORS

	Risk Factors	Associated Cancer(s)	Scientific Evidence
1	Passive smoking (e.g. non–smoking wives of smokers and others who involuntarily breathe in the smoke of other's cigaretes)	Lung cancer cancers of the mouth, nose, pharynx, oesophagus, bladder and pancreas.	Epidemiology. [32, 33] Mechanism. See Fig. 4
2.	Over–exposure to sunlight in children less than 10yrs (especially within the peak hours of 10.00 am to 3.00p.m), in adults or children who play or work around sand or concrete surfaces which reflect up to 85% of U.V. rays or who live at high attitudes.	Skin cancers (mainly basal and squamous cell carcinoma	Epidemiology and Experiments with U.V. rays. [34, 35] Mechanism: induction of mutation leading to malignant transformation of target cells.
3.	Exposure to electric and magnetic fields in one's work place or in the vicinity of over–head high tension wires.	Leukaemia	Epidemiology[36] Mechanism. interference with mitotic process of rapidly dividing cells by electromagnetic waves.

TABLE 1(e) – IATROGENIC RISK FACTORS

	Risk Factors	Associated Cancer(s)	Scientific Evidence
1.	Radiotherapy for:	Head and neck	
(a)	Tinea capitis	cancers	
(b)	Vascular naevi and pituitary adenoma	Meningioma and primary malignant sarcoma.	Human case studies, [37, 38]
(c)	Acute lymphoblastic leukaemia.	Brain tumours	Mechanism. Induction of gene mutation which could lead to malignant transformation of target cells.
(d)	Recurrent ganglion neuroblastoma	Leiomyosarcoma of the great vessel of the neck.	
2.	Surgical iatrogenic factors such as: venepuncture/intravenous infusions, and abuse of parenteral injections.	Primary hepatocellular carcinoma	Epidemiology.[39] Mechanism. See Fig. 5
3.	Exogeneous estrogen therapy for post menopausal or post oophorectomy patients.	Endometrial and Breast cancer	Human case studies and Epidemiology. [40, 41] Mechanism: Induction of abnormal hyperplastic activity.
4.	Prolonged intake of oral contraceptives	Cancer of the extrahepatic duct system, hepatic Adenoma, hepatocellular carcinoma	Epidemiology. [42, 43] Mechanism: Unknown

Fig. 5 – (Some surgical iatrogenic factors and the risk of primary liver cancer)

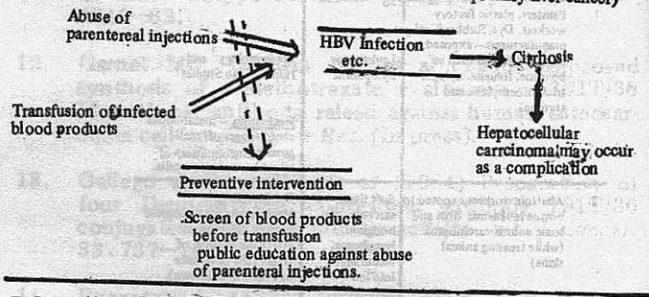
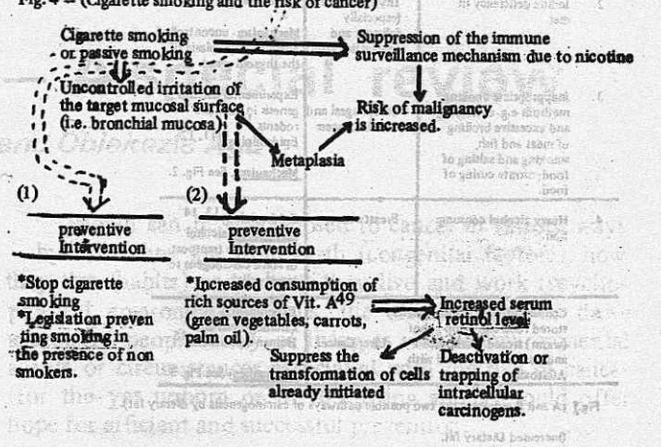


TABLE 1(f) – SOCIAL/BEHAVIOURAL RISK FACTORS

	Risk Factors	Associated Canser(s)	Scientific Evidence
1.	Sexual promiscuity especially among those with many male or female sexual partners (with the associated risk of STD due to Human papilloma virus. syphilis, gonorrhoea, chlamydia and Herpes simplex virus).	Squamous neoplasm of the male or female genital tract (especially cancer of the cervix).	Animal experiments and Epidemiology. [44, 45, 46] Mechanism: Chronic infections lead to metaplastic changes in the affected epithelium as well as to reduced immune surveillance system.
2.	Cigarette smoking (especially by people exposed to inhalation of asbestos dust).	Lung cancer cancer of the bladder and kidney.	Human case studies, Epidemiology and Animal experiments.[47, 48] Mechanism. See Fig. 4.

Fig. 4 – (Cigarette smoking and the risk of cancer)



DISCUSSION

This review shows that a lot of work has been done in recent years on how best to stop the life–threatening intractable disease–cancer. The risk factors enumerated from the reviewed journals are not however encompassing; notable risk factors left out include exposure to nuclear radiations and poor environmental sanitation. The latter is very worthy of mention in this work as it could be strongly implicated in the aetiology of most malignancies in the poorly developed parts of the world.

The role of poor environmental sanitation in carcinogenesis was highlighted many years ago by Ferguson (1907,11) when he attributed the malignant disease of the urinary bladder to the prevalence of urinary Bilharziasis.[50]

The mechanism of pathogenesis (A,B,C) is illustrated in Fig. 6. There is also an association between chronic *schistosoma* japonicum infection and Hepatoma formation.[51]

The detailed mechanism of carcinogenesis of most of the risk factors outlined is needed for a more targeted preventive measure, but has predominantly remained a mystery. However a closer look at all the risk factors shows that the application of feasible aspects of the principles of cancer prevention can appreciably reduce the incidence, morbidity and mortality of cancer.