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BIOCHEMISTRY FOR THE HEALTH OF MAN

By

Prof. J. B. Fakunle
Professor of Biochemistry

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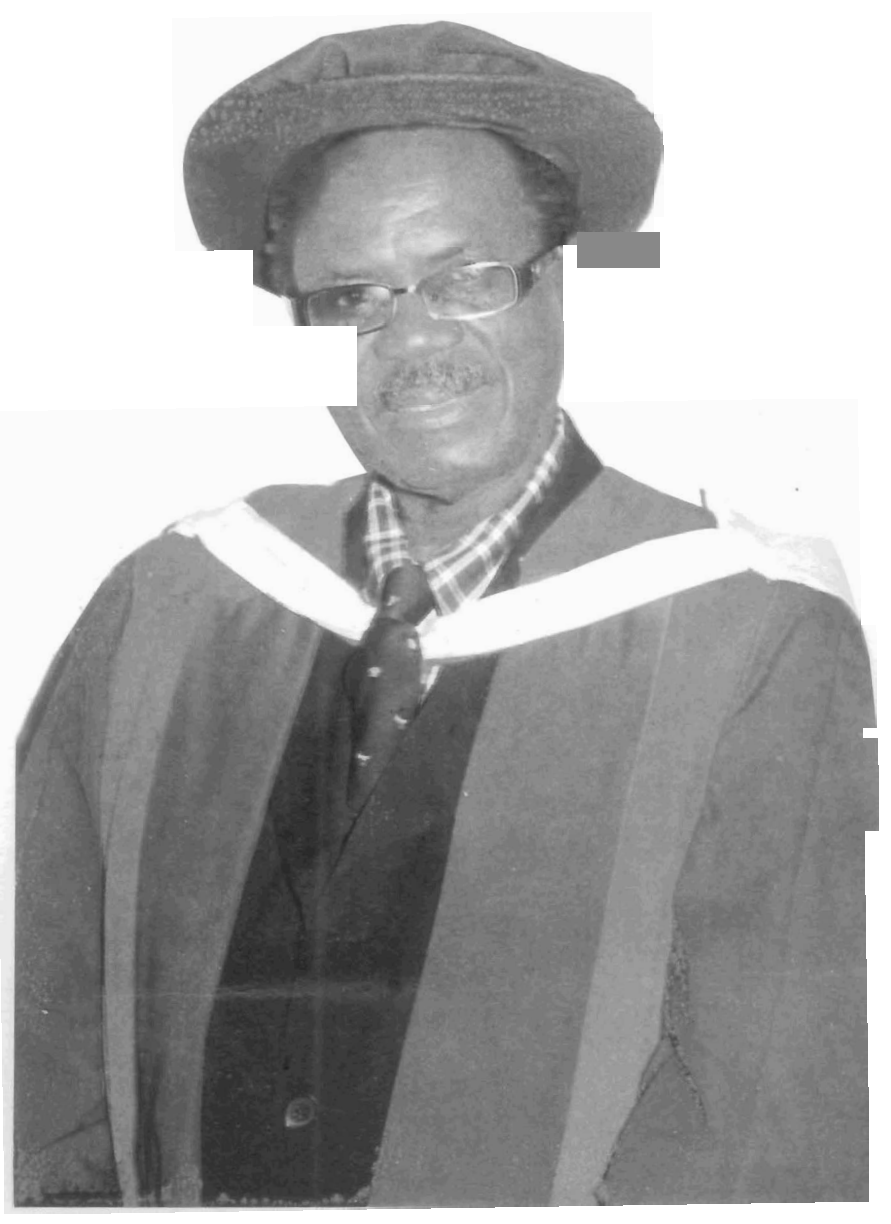

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An Inaugural Lecture Delivered at Oduduwa Hall, Obafemi Awolowo University, Ile-Ife, Nigeria on Tuesday 25th June, 2013

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INTRODUCTION

The Vice-Chancellor sir, distinguished ladies and gentlemen, I am exceedingly happy to stand before you today to deliver this inaugural lecture, being the first to be delivered in the newly created Department of Medical Biochemistry. The Department of Chemical Pathology was created on the 1st August, 1983. Few months later, Professor S O. Olusi delivered an inaugural lecture titled. "Cancer in our society" on the 15th November, 1983. Today, I am delivering a lecture titled "Biochemistry for the Health of Man". Three years after the Department of Medical Biochemistry was carved out of the Department of Chemical Pathology.

After my training in Medical Biochemistry at Howard University, Washington, D.C., I was recruited by the National Universities Commission for the Department of Biochemistry at Ahmadu Bello University, Zaria. The Department, domiciled in the Faculty of Science teaches students in the Faculties of Medicine, Pharmacy, Veterinary Medicine and Science. As one of the teachers of the medical students, I represented my Department in the Faculty of Medicine throughout my stay in the institution.

In 1985, I was offered an appointment in the Department of Chemical Pathology of this University to teach Medical Biochemistry in the College of Health Sciences. Before December 2010, the Department of Chemical Pathology here in Ife, taught both Medical Biochemistry and Chemical Pathology to four professional programs, namely: Medicine, Dentistry, Nursing and Medical Rehabilitation. I have since 1985 with other colleagues taught Medical Biochemistry to Medical, Dental, Medical Rehabilitation and Nursing students in our College of Health Sciences. I have also actively participated in the training of Postgraduate students in my Department as well as the Departments of Anatomy and Cell Biology and the Department of Physics in the Faculty of Science. I have for more than twenty years cooperated with my friend, Professor J. B. Olomo, a

distinguished Professor of Medical Physics in the training of Medical Physicists; I worked with Professor J. O. Fawole, another friend in the Institute of physical Education, Faculty of Education, on Diet, Nutrition, Sports and Exercise Physiology and we supervised a doctoral dissertation in this area. I also joined research efforts with a Professor of Microbiology in the Faculty of Science, Professor P. O. Olutiola and we jointly supervised a Master Degree thesis and two Doctoral Dissertations. Several reports describing our research have been published in scientific and professional journals.

Our programme in Chemical Pathology is a composite of several disciplines where teaching and research have their primary orientation to human diseases and where responsibility is accepted for the large segment of Laboratory Medicine which is the applied field of the professional clinical Chemist and Medical Biochemist. Chemical Pathology (Clinical Biochemistry) is unique in having to blend together Analytical Chemistry, Biochemistry, Biophysics, Pathology, Physiology and Immunology as well as other disciplines. All these are required to maintain and improve laboratory services for patient care.

The Clinical Chemistry Laboratories in our Teaching Hospital are the practical expression of all that is known about Biochemistry of disease processes. To support these laboratories, our aims in the Department are to:

1. Accumulate and integrate knowledge across diverse areas of Clinical Biochemistry and teach what is relevant to an understating of human diseases and the role of Clinical Chemistry Service.
2. Advance our knowledge through research into the mechanisms of diseases and research directed at improving the diagnostic capacity of the service laboratories.
3. Foster the development of research capabilities and provide professional training in Clinical Biochemistry.

In order to fulfill these objectives, we seek to maintain a staff of scientists with both medical and non-medical backgrounds relevant to the discipline of Clinical Biochemistry. We also believe that neither good teaching nor applied research can be sustained without an ongoing programme of sound basic research.

Consequently, strong emphasis is placed on our postgraduate programmes leading to the Master of Science and Doctor of Philosophy Degrees.

BIOCHEMISTRY

Biochemistry is the chemistry of life. It is the study of substances found in living organism, the changes they undergo during development and life of the organism, and metabolism by which energy is made available for live processes and for synthesis of various complex molecules. Biochemistry is one of the cornerstones of modern scientific Medicine, Pharmacology, Pharmacy, Physiology, Nutrition, Genetics, Pathology, Toxicology and Microbiology: It is therefore relevant to the definition of health and investigation of diseases. Furthermore, it is important to Zoology, Botany, and Agriculture as well as other Biological Sciences. The Knowledge of Biochemistry is essential to all life sciences and it is actually increasingly becoming their common language (White, *et al* 1978; Murray, *et al* 2003).

Biochemistry has profoundly touched on man's health and wellbeing and on our understanding of the catalytic processes taking place in the metabolism of living organisms. For example the relationship between diet and disease was discovered in antiquity. Organ meat such as liver has long been known to cure night blindness. At that time, one wondered or marveled how this could be. Today, we know that liver is a good source of vitamin A. In the eighteenth century cod liver oil was first used to treat rickets. Today, we know that cod liver oil is a good source of vitamin D. Juice of limes was discovered to prevent the symptoms of scurvy (caused by vitamin C deficiency) among the seamen of the British

Navy. Because of this, British sailors came to be known as "limeys". Today, we know that juice of limes is a good source of vitamin C.

In 1912, F. G. Hopkins, in England, proved experimentally that animals require more than protein, fat and carbohydrate in the diet for normal growth. He therefore postulated that one or more accessory factors present in certain natural foods were necessary in the nutrition of animals. In the same year, Casimir Funk obtained a concentrate of an amine from rice husks and polishings that alleviated the symptoms of the disease beriberi, prevalent among Japanese sailors limited to a diet of milled or polished rice. At that time, he coined the word (vita amine), denoting an amine essential to life (today spelled vitamin, since many of the substances in these classes are not actually amines). Shortly thereafter, it became clear that there must be several vitamins, when E. V. McCollum, in the United States, discovered that young rats require both fat soluble and water soluble growth factors which are today called fat and water-soluble vitamins. Acquisition of sound knowledge of Biochemistry is necessary for health professionals because Biochemistry deals with two major concerns namely: the understanding and maintenance of health and the understanding and effective treatment of disease. Biochemical studies have illuminated many aspects of health and disease, and conversely, the study of various aspects of health and disease has opened up new challenges of Biochemistry (Lehninger, A. L. 1975, Murray *et al* 2003).

MY RESEARCH ACTIVITIES

I have had the privilege of performing the dual role of teaching and conducting research in several Universities. My research forage has always been in the field of Biochemistry of diseases and I have initiated and implemented most of these research activities in collaboration with other colleagues. The hallmark of these research

endeavours has its relevance and pertinence in the promotion of Health.

RESEARCH CONTRIBUTION IN HYPERTENSION

Hypertension or elevated blood pressure is a serious public health problem that affects millions of people all over the world. Studies have demonstrated a higher incidence of the disease in blacks than their caucasion counterparts (Laragh, 1974; Cheitlin, 1974; Sheps, 1975 and Nies, 1977). However, in urban population of African communities the incidence of the disease is about the same as that of black American (Okoron, 1977 and Milne, 1978), but on the whole the incidence is less among the African population (Johnson, 1955, 1963). It has been estimated that hypertension is responsible for many deaths and is an important contributor to more than a million fatal myocardial infarcts and cerebrovascular accidents (Laragh, 1974 and Nies, 1977).

There is no evidence of a threshold level for the development of complications, but according to the World Health Organization (WHO) criteria 160mmHg systolic and 95mmHg diastolic and above are considered in the hypertensive range, while 140mmHg systolic and 90mmHg diastolic has been referred as borderline or possible hypertension (Nies, 1977; Okoron, 1977; Ostfeld, 1978 and Milne 1978).

Hypertension or high blood pressure is a hemodynamic abnormality which may result from the derangement of cardiovascular dynamics (Braunwald *et al* 1963, Selkurt 1972 and Nies 1977). This hemodynamic abnormality is most often perceived as an increase in the peripheral resistance of arterioles and smaller arteries. High blood pressure can either be primary or secondary (Selkurt, 1972; Jagger and Braunwald, 1977 and Nies, 1977). In the case of primary hypertension, the etiology is still unknown and this represents about 90-95% of hypertension cases, whereas, secondary hypertension may result from conditions such

as pheochromocytoma, cushings syndrome and renal artery stenosis (Selkurt, 1972 and Jagger, *et al* 1977).

It has been conclusively demonstrated that patients are tremendously benefited by the therapy of antihypertensive agents (Briggs, 1965; Veterans, 1967; 1970 and Nies, 1977). Drugs are administered singly or in combination in accordance with the severity of the disease (Selkurt 1972). Generally, a diuretic regimen is first established for a patient. If this procedure does not achieve the lowering of the blood pressure that is needed, the practice is to combine diuretics with other more potent antihypertensive drugs. The dosage level of antihypertensive drugs varies from patient to patient. Some patients require a larger dosage of a given drug to produce the same blood pressure depression (Sheps, 1975 and Tobian, 1975).

To be effective, the drugs must be titrated to their near optimal dosage (Sheps, 1975 and Tobian, 1975); above all, monitoring of patients compliance to the therapeutic regimen is crucial to effective drug therapy (Francis, *et al* 1969; Caldwell, *et al* 1970; Mazzulo *et al* 1972; Mushlin *et al* 1972; Blackwell, 1973 Cheitlin, 1974 and Sheps, 1975). This can only be done if proper analytical methods for the assay of drugs in body fluids or tissues are developed. This was the basis of my research collaboration with Professor Willie Ruff of the Department of Pathology, Clinical Laboratories of Howard University Hospital. We developed methods using thin layer chromatography, ultraviolet spectrometry and gas liquid chromatography/mass spectrometry to detect the presence of commonly used antihypertensive drugs in biological fluids such as urine and plasma. By developing these methods which are reliable, simple and fast, we were able to introduce drug monitoring into routine service for the improvement and optimization of patient care and thereby aid physicians in the intelligent management of their hypertensive patients (Fakunle, 1979; Ruff, Fakunle, 1979 and Ruff, Fakunle, 1980).

RESEARCH CONTRIBUTION IN CANCER

Cancer is an English word derived from a Greek word "Karkinos". Cancer is synonymous with tumor or neoplasm. In Greek neoplasm means new growth. Cancer (Malignant tumor) can be defined as a malignant new growth anywhere in the body of a person or animal which can exhibit the properties of invasion and metastasis. Cancer tends to spread locally and to distant parts of the body. Cancer can be divided into five broad categories namely: carcinomas, sarcomas, leukemias, lymphomas and melanomas. Cancer Cells are unrestricted and uncontrolled in their growth. They have the capacity to:

(a) invade the surrounding tissues.
(b) destroy contiguous normal cells.
(c) Exhibit the properties of invasion and metastasis i.e. they break away from their parent colony and travel via lymph or blood to distant sites where they develop secondary colonies.
(d) Lose their normal histological appearance and biological character i.e. both cells and tissue characteristics change (WHO 1975, Vasudevan, *et al* 2008 and Chatterjea, *et al* 2008).

Oncologists (specialists in the study and treatment of cancer) are of the opinion that some forms of cancer are caused by genetic factors, while others are caused by environmental conditions. In other words one patient may already have a family history of breast cancer while another was exposed to a carcinogenic chemical in a factory. Both suffer cancer- the only difference is the root mechanism which triggered the abnormal cell growth. Because cancer begins at the microscopic cellular level, the first signs of a malignant growth are nearly impossible to detect without special tests and training. In the case of pancreatic cancer, for example, there is little to no pain involved as the first malignant cells form around the organ. As the tumour becomes more organized new

blood vessels may form to feed it directly or older vessels may be diverted. Meanwhile, the host body may only experience a few symptoms which resemble many other conditions besides cancer. Only after a sample of suspicious tissue has been removed and tested (biopsied) can many cancer forms be diagnosed (Weisburger, *et. al* 1966 and WHO 1975)

The most widely adopted methods of treating cancer is surgery, radiotherapy and chemotherapy. These methods are not only capital and technology intensive, they are not without other deleterious consequences. For example chemotherapeutic agents are toxic and hence affect the nutritional status of patients and the therapy reduces the body resistance to infection. The need to develop a less painful and safer alternative for cancer therapy has become an obvious challenge in medical research. To find a possible alternative to surgery, radiation and toxic chemical therapy, our group (Fakunle, *et al,* 1982, Crisis, *et al,* 1983; Dhillion *et al,* 1982; Fakunle, *et al*, 1993) prepared extracts from several members of the lily family and other food plants (Table 1). The extracts were tested in several *in vivo* and *in vitro* systems and a dietary aqueous extract from fresh members of these lily family and other food plants inhibited the growth of *Moris Hepatoma* 3934A and inhibited the activity of the hepatoma enzyme, *Guanylate cyclase.*

It has been established that elevated levels of cyclic guanosine monophosphate (cGMP) are observed in cells undergoing rapid proliferation including cancer cells, inhibition of the enzyme *Guanylate cyclase* which is the only enzyme known to produce cGMP, should theoretically allow decreased levels of cGMP and thus decrease cellular growth. Extracts from the plant called balsam pear *(Momordica Charantia)* have been observed to inhibit this enzymatic system and to inhibit the growth of cancer cells in culture (Vesley, *et al* 1977).

Garlic *(Allium sativum)* has been said to exist before the written languages of man (Health Research, 1978). Numerous reports from 6000BC (China), 4000 BC (India), and 3500 BC (Egypt) indicate that garlic was used as a food vegetable and as a medicinal plant (Airola, 1971, 1977, 1978 and Health Research, 1978). Hippocrates, the father of Medicine, listed garlic as first in his herb codex of Medicines (Airola, 1971, 1977, 1978) while Dioscorides, Surgeon General of Roman armies, used huge quantities of garlic to prevent and treat a wide variety of diseases of his legions (Airola, 1971, 1977, 1978). In modern medicine, garlic is mainly employed as a germicide, antiseptic, for intestinal disease and for high blood pressure (Airola, 1977 and Passwater 1977). Sulfur-containing organic compounds such allicin, extracted from garlic, have preventive and/or healing properties for a variety of diseases (Brahamacharie, 1962; Prasad *et al* 1966, and Weisburger, *et al* 1957).

Because reports indicated that garlic might contain substances with anti-cancer properties (Weishburger et al 1957), we began a series of studies in our effort to evaluate this possibility. Positive correlations were observed using specific purified garlic extract (Table II) between the inhibition of the enzyme *Guanylate cyclae (in vitro)* and the growth of *Morris Hepatoma* 3934A *in vivo* (Tables II and III) (Fakunle, *et al* 1982 and Crisis, *et al* 1982, Dhillion, *et al* 1981).

In Table III it was observed that garlic significantly inhibited the growth of Morris hepatoma 3934 A when supplemented in the diet at levels 2.5 and 5%.

The extracts were purified by sephadex G-25, DEAE cellulose, and isoelectrofocusing chromatographies to yield a potent inhibitor of hepatoma *Guanylate cyclase,* the only enzyme known to produce the growth regulator, cyclic GMP. This inhibitor which was a polypeptide near 10,000 daltons in size, was stable at pH 3.5, had an isoelectric point near 2.5 and altered the maximum velocity

(Vmax) and Michaelis Menten Constant (Km) of the enzyme. It was therefore concluded that the inhibition of tumour growth by garlic extract feeding may result from the reduction of tumour cyclic GMP levels.

TABLE I. Identification of *Guanylate cyclase* inhibitors in several food plants.

Food Plant	*Percentage inhibition of Guanylate cyclase in vitro*
Garlic	89.9*
Asparagus	93.8*
Kale	93.1*
Scallion	70.1*
Leeks	82.9*
Onion	83.5
Broccoli	45.2*
Cabbage	15.1
Lettuce	0.0
Yellow squash	0.0
Green squash	0.0
*P<0.01	

TABLE II. Summary of the purification of *Guanylate cyclase* inhibitor from garlic

	Units of inhibitor activity[1]
Boiled and centrifuged extract	850
Sephadex chromatography	150
DEAE cellulose chromatography	26
Isoelectrofocusing chromatography	10

Summaries of the purification of the garlic extract. Final purification produced a protein inhibitor with the following characteristics: molecular weight of 8000A, heat stable, acid-stable, protease-resistant, isoelectric point of 4.5 and kinetically non-competitive with respect to cGMP.

[1]*Activity defined as microgram of protein inhibitor necessary to inhibit 50% of added hepatoma guanylate cyclase activity.*

TABLE III: Effect of garlic extract dietary supplement on the growth of Morrishepatoma 3924A

S/No	*Experimental groups*	*Tumour size, cm*^{2}
1	Minus garlic	29.8 $\pm$ 1.6*
2	Plus 2.5% garlic	22.6 $\pm$ 1.3*
3	Plus 5% garlic	15.7 $\pm$ 1.1*
* $p < 0.01$		

The garlic extracts significantly inhibited the growth of *Morris Hepatoma* 3924A, when supplemented in the diet at levels of 2.5 or 5%.

Aside from natural substances, we also used some drugs such as aspirin and indomethacin in our effort to find alternative to surgery, radiation in the treatment of cancer. It has been documented that inhibition of prostaglandin biosynthesis by aspirin and indomethacin correlates with the reduction in tumour growth (Bourne, 1974; Pelus, *et al,* 1977, Goldyne 1977 and Moncada, *et al* 1980). The effects of aspirin (salicyclic acid) and indomethacin on the growth of cancer *(Morris Heapatoma* No 7800) were investigated.

Tumour areas and weights were significantly reduced by aspirin supplemented diet ($p < 0.01$, Table IV, figure 1). At a higher concentration of dietary salicylic acid (0.75%), the inhibition of tumour area ($12.2 \pm 1.0 cm^2$) and the weight ($13.5 \pm 1.0 g$) was greater than the inhibitory effects of the drug at the lower level. The area of the tumours ($18.4 \pm 12.2 cm^2$) and the weights of the tumours ($20.3 \pm 3.2 g$) from the animals that were fed the diet supplemented with 0.5% salicyclic acid were significantly higher than comparative values of the animals which were fed diets containing 0.75% salicyclic acid ($p<0.01$).

Our work also showed that diets supplemented with these drugs slowed the growth of cancer with biochemical investigations indicating no symptoms of toxicity and renal damage in the rat (Knight, Fakunle and Criss, 1983; Knight, Fagbemi, Fakunle and Criss, 1984).

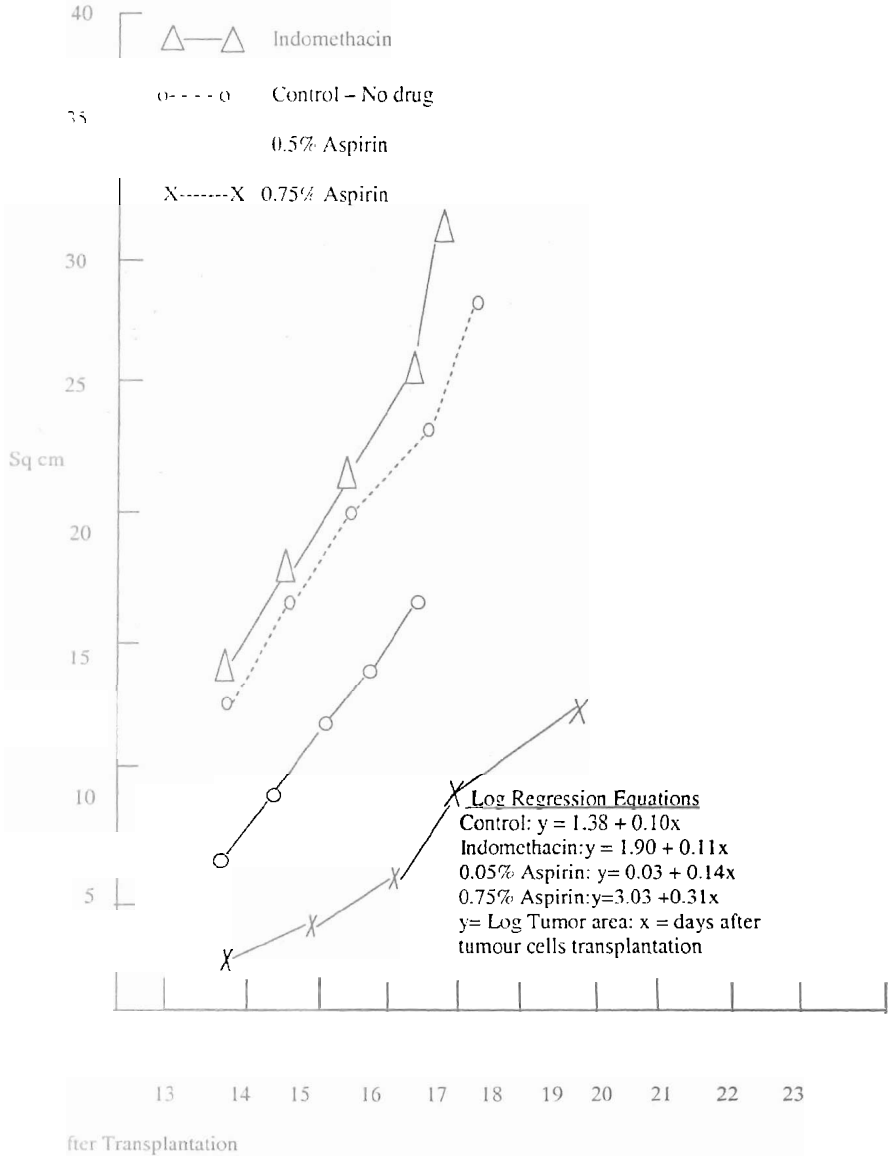
TABLE IV: *The effects of aspirin and its derivatives on the Growth of Morris Hepatoma No. 7800*

Experimental groups	*Number of Animals*	*Type of Drug*	*Amount of Drug%*	*Tumor Weight (g)*	*Tumor Area cm^2*
1	9	None	None	39.3 ± 3.3^a	31.5 ± 0.9^a
2	9	Indomethacin	0.003	39.1 ± 1.8^a	33.1 ± 1.7^a
3	8	Salicyclic Acid	0.50	20.3 ± 3.2^b	18.4 ± 2.2^b
4	9	Salicyclic acid	0.75	13.5 ± 1.0^c	12.2 ± 1.0^c

All values = Mean $\pm$ SEM

Means with unlike superscrips are significantly different ($p<0.01$)

Effect of Aspirin on cancer growth



: TUMOUR AREAS OF RATS ON DRUG DIET

RESEARCH CONTRIBUTION AT ZARIA.

At Ahmadu Bello University, Zaria, I joined other colleagues in conducting some research aimed at improving the health of Nigerians. This included research on Nigerian patients with lepromatous leprosy and formulation of infant weaning food for the prevention of protein energy malnutrition.

(A) Nigerian Patients with Lepromatous Leprosy.

Leprosy is an infectious disease of man caused by the bacteria *Mycobacterium leprae* (M. Leprae) (Woodruff, 1974). It is a problem of enormous dimension in many countries including Nigeria, in the topics and subtropics (Reddy, et al, 1985, Noorden, 1985). It occupies a unique place among communicable diseases because of the incidents of deformity and physical handicap with serious social and economic implications.

Available evidence suggested that accumulation of vast numbers of bacilli *(M.Leprae)* in infiltrated host cells play an important role in lepromatous leprosy (LL) patients (Godal, 1984). It is speculated that due to an immunological defect, remarkably specific to M. leprae, the defence system fails to attack the leprosy bacilli which are thriving in the tissues in large numbers (Godal, 1984). Modern immunology has established that a successful and a specific immune response in a host occurs as a result of complex interaction among thymus derived cells (T.Cells), bursa or bone-marrow derived cells (beta-cells) and antigens presenting cells (APC) (Roitt, 1984; Benacerraf *et al,* 1979). One of the main ways that this tripartite interaction may take place is through cell-cell contact via plasma membranes. The cellular plasma membranes are composed of lipid bilayers into which various proteins, cell surface antigens and receptors are embedded (Marchesi,1978). Any alteration in the biochemical composition of the lipid bilayers of the plasma membrane of any one cell type (T, B or APC) may, therefore, influence the outcome of the complex tripartite interaction. Some investigators have indeed reported definitive

changes in lipid metabolism in leprosy patients (Kusaka, 1958; Vankatesan *et al* 1978; Scritharan *et. al* 1979). Also there are evidences that certain diseases where generalized membrane defects were observed, parallel defects were detected in the red cell membrane as well (Godin, *et, al.,* 1978; Godin, *et al,* 1981; Chan, *et al,* 1983). Based on this reported information, our group went ahead to examine the lipid parameters of some lepromatous leprosy patients in the Zaria region of the Kaduna state. Our studies showed that total lipid, total cholesterol and total triglyceride contents in the patient's erythrocyte membrane were similar to those in the control subjects. However, the amount of total phospholipid was observed to be significantly lower in the patients than in the control subjects ($p<0.05$) (Akwu, Fakunle, and Giassuddin 1986).

Cholesterol is one of the major and important components of plasma membrane from structural and functional point of view, whereas triglyceride concentration in the membrane is quite small (Vandenheuvel, 1963; Bruckdorfer, *et al* 1969). No significant alterations in these two components were observed in our studies, however because of the reported importance of phospholipids for structural and functional integrity of the membranes in a variety of biological systems (Inoue, *et al,* 1971; Waite *et al,* 1969; Giassuddin, *et al,* 1981), we proposed that membrane phospholipid deficiency may lead to structural distortion of the plasma membrane as reported in our studies (Akwu, Fakunle, and Giassuddin 1986).

NIGERIAN WEANING DIETS AND NUTRITIONAL BIOCHEMISTRY

Many Nigerians especially the pre-school age group suffer from Protein Energy Malnutrition (PEM) causing permanent brain damage and learning capability. Surfeit of dietary protein to this vulnerable group will alleviate this suffering and improve the diets of these Nigerians. Our group directed our research activities

towards improving the health of these groups of Nigerians by formulating weaning diets from our available local foods stuffs.

FOOD SUPPLEMENTATION FOR WEANING INFANTS.

Weaning is that period from the end of complete breastfeeding until the infant is entirely placed on adult diet (Buchanan, 1975). The Weaning period is a delicate period in the life of an infant during which the child is still growing rapidly and has just ceased from benefiting from the maternal protective antibodies (Olfat, et al., 1982). Adequate supplementary feeding during the first years of life has been shown to prevent malnutrition and its consequences in the formative years (Evans, *et. al* 1971).

Protein Energy Malnutrition (PEM) is on the top priority list of the nutritional diseases. It also includes avitaminosis which increases the susceptibility of the infants' body to certain infectious diseases such as measles, pneumonia and tuberculosis (Simic, 1969). Prominent causes of PEM are faulty food habits, ignorance, poverty, unavailability of rich protein sources, large family size and inadequate sanitation (Ojofeitimi, 1982). Although clinical syndromes present themselves between the ages of one and a half to three years, the process of under-nutrition begins around the age of six months. Protein energy malnutrition has been shown to be a leading health hazard in Nigeria (Editorial, 1983).

Legumes, cereals, grains and nuts have been found to provide a large part of the calories and proteins for most people in Africa, Asia and Latin America. It has been reported that when grain legumes are combined with cereals, they provide an almost ideal level of dietary protein for humans (Arroyave, *et al.*, 1961). Nigerian infants are traditionally weaned on the Ogi (Yoruba), a maize gruel in the Southwestern part of Nigeria, while Akamu (Hausa), a sorghum gruel was adopted in the Northern areas. Research reports have proved that such diets could not support infants' rapid growth, thus leading to the prevalence of PEM

among these communities. Each of these cereals (maize and sorghum) has been supplemented with grain legumes, soyabean and cowpea respectively (Akinrele, *et. al*, 1970; Oyeleke, O. A. 1981).

Our group intensified research towards producing low cost high protein and energy supplemented foods that could easily be available at the village level. Weaning infant food from local materials cowpea, sorghum, and banana was formulated using simple and locally available technology (Odetola,1975).

The nutritional parameters for protein quality, such as Net Protein Utilization (NPU), Protein Efficiency Ratio (PER), Biological Value (BV) were evaluated. Results showed that the processed formula favourably compared with commercial cerelac. Our research efforts proved that simple technology could be employed to process the locally available raw materials as infant weaning food at the village level in Nigeria.

BIOCHEMISTRY FOR THE HEALTH OF NIGERIANS – SOME CONTRIBUTIONS FROM IFE

My Department has made enormous contribution to knowledge in the areas of Clinical and Nutritional Biochemistry. Our research contributions at Ife have relevance and pertinence to the promotion of the health of Nigerians. We conducted biochemical research relating to oncology, sickle cell anaemia, PEM, HIV/AIDS, Prostaglandins and infertility, as well as Hypertension in pregnancy.

(a) Research in Oncology

We conducted research to identify simple biochemical markers for early detection and diagnosis of common malignancies in Nigeria in an attempt to aid physicians and other health professionals in the intelligent and effective management of their cancer patients. Cholesterolaemia has

been reported in hepatoma patients and this is known to be due to the absence of sensitive feedback regulation for cholesterol biosynthesis. Our findings have led to the conclusion that serum cholesterol levels can be used in distinguishing metastatic from non-metastatic cancers (Ogunleye, Fakunle, Odewumi, 1989). Also, as a result of various claims that serum acid phosphatase can be employed as an aid in the diagnosis and management of advanced carcinoma of the prostate, a study was conducted to investigate the serum levels of tartrate-labile acid phosphatase in prostatic and non-prostatic malignant and non-malignant diseases in Nigeria population. Our results suggest that enzymatic method of prostatic phosphatase estimation may not be useful in discrimating patients with prostatic cancer from those suffering from other diseases (Ogunleye, Fakunle, Ajeneye and Oyeleke, 1991).

Research in Sickle Cell anaemia.

Sickle Cell anaemia affects several tissues of the body (Brown et at 1972). The chronic jaundice is a reflection of hepatobiliary involvement and the skeletal system. This is shown by an increase in the size of marrow cavities and death of bone because of blockage of blood supply and an increased incidence of osteomyelitis (Rosenblate, *et al*, 1970; Thomas, *et al.* 1980).

Alkaline phosphatase, a membrane related enzyme is found in both liver and bone marrow (Moss, 1982). An alteration in the activity of this enzyme in serum in sickle cell anaemia has been reported in adults (Brown, *et al,* 1972). Our group therefore decided to estimate the activity of this enzyme from patients with sickle cell anaemia in a paediatric population at Ife. Our findings showed that the activity of alkaline phosphatase was significantly higher ($p \leq 0.05$) in sickle cell children than in healthy controls.

One interesting discovery of this investigation was that two patients, a male and a female having vaso-occlusive crises at the time of blood collection were included in the study and their alkaline phosphatase activities in serum were 835.5 u/L and 692.8u/L respectively; This activity was particularly very high apparently because vaso-occlusive crises are known to occur during the course of sickle cell anaemia and might be due to infection (Brown, *et al* 1972). We therefore concluded that the extremely high activity of serum alkaline phosphatase during the crises may be of clinical importance (Ogunleye, Adeleke and Fakunle, 1990).

Chronic haemolysis and tissue necrosis are two common features in sickle cell disease. Lactate dehydrogenase (LDH) has been frequently employed as a diagnostic tool in diseased states associated with tissue destruction (King, *et al*, 1952; Phillipi, *et al* 1961; Kunni *et al,* 1964). Our groups therefore decided to investigate LDH as an enzyme marker for a population of sickle cell anaemia children in Ile-Ife region. The study revealed that haemolysis and liver necrosis are responsible for elevation of lactate dehydragenase in the sera of sickle cell anaemia patients (Ogunleye, Adekile and Fakunle, 1991).

(c) Research on Prostaglandins

The Department of Chemical Pathology initiated and pioneered the prostaglandin research in the College of Health Sciences. In doing so, we joined research efforts with our colleagues in the Department of Obstetrics, Gynecology and Perinatology.

Prostaglandins (PGS) are in the family of fatty acid derivatives which have a lot of potent biological activities of hormonal or regulatory nature. Prostaglandins, discovered initially in the seminal plasma by U.S Von Euler, a Swedish physiologist in the

1930s are now synthesized in every tissue of the body. There are two main sets of prostaglandins, the E and F series, each having three members, E1, E2 and E3 with F1x, F2x and F3x. Therefore there are six primary prostaglandins namely; PGE1, PGE2 PGE3, PGF1x, PGF2x and PGF3x. In addition to the six primary prostaglandins, there are several secondary ones, most of which are products of enzymic or chemical dehydrations of the PGEs (White *et al*, 1978, Euler 1934; Euler, 1935, and Euler, 1936).

Prostaglands have a wide range of biological actions involving cardiovascular effects, renal effects, nervous system effects, metabolic effects, water and electrolyte effects, gastrointestinal effects, bronchial, tracheal and smooth muscle effects, inflammatory effects, Immune effects, skin effects, eye effects and on reproductive organs. The potential possibilities of the clinical uses lie in the areas of peptic ulcer, hypertension and obstetrics and gynecology (fertility control, abortion and induction of labour). (White, *et al* 1978, Bhagavan *et al* 1976).

With a Research Grant (Research Code 11713 AFH) "Prostaglandin levels in partners of infertile women and their relationship to semen quality in Ile-Ife" from the University Research Committee (URC), we collaborated with the Human Reproductive Unit, Medical Research Council, Edinburgh in the United Kingdom and embarked on a Research on Prostaglandins and fertility control in Ile-Ife and its environs to achieve the following:

1. Measurement of prostaglandin levels in men with normal semen parameters
2. Measurement of prostaglandin levels among oligospermic and azoospermic partners of infertile couples attending Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife.

3. Establishment of possible relationships between prostaglandin levels and various parameters of semen quality.
4. Establishment of possible relationships between prostaglandin levels and socio-economic status.

Eleven percent of our respondents were azoospermic, 43.9% oligospermic and 44.7% normospermic. The mean total PGE levels in fertile group (325.1 ± 28.3 ug/ml) was significantly higher than in the infertile group (225.1 ± 15.1ug/ml) ($p< 0.05$). The mean PGF2x level in the fertile group (2.1 ± 0.32 ug/ml) was significantly lower than the infertile group (3.0 + 0.28ug/ml) ($p<0.05$). The mean PGE concentration in the normospermic group (301.3±215ug/ml), the oligospermic group (216.81 ±19.1ug/ml) and the azoospermic group (168.7 ± 29.7 ug/ml) differed significantly ($P<6.05$).

Also, PGF2x in the three groups normospermic, oligospermic and azoospermic (2.23 ± 0.23 ug/ml, 3.45 ± 0.42 ug/ml, and 2.06 ± 0.43 ug/m^1) respectively differed significantly ($p<0.05$). Men in the high socio-economic status and those who had high PGE values tend to have overall better semen parameters results when compared to others. Our study concluded that routine screening for male infertility should include measurement of both PGE and PGF2x levels in semen (Emma-Okon, Fasubaa, Fakunle, 2011).

(d) Protein Energy Malnutrition

Protein energy malnutrition as earlier mentioned in this lecture is one of the causes of morbidity and mortality in Nigerian children. Lack of protein, energy, vitamins and minerals particularly iron resulting in iron deficiency anaemia with low packed cell volume (PCV) and he moglobin concentration are common etiologies (Adam *et al* 196-, Mcfarlane, *et al;*, 1970, Olusi, *et al*; 1979 and Caballero, *et al*, 1983). In a study conducted by our group at Ife in the Dietetic department of the OAUTHC twenty energy malnourished children, five for kwashiorkor (K), five for marasnus

(M), five for Marasmic – kwashiorkor (M-K) and five for undernourished children (U) aged between one and five years were admitted into the peadiatric ward of the OAUTHC. They were hospitalized for 18 days. The hospital diet for K and M-K consisted of 8% protein and 802 calories per litre while that for M and U consisted of 30% protein and 1350 calories per litre. After a period of 18 days of rehabilitation, there was no significant ($p< 0.05$) difference in the weight for age. None of the haematological parameters were significantly different after rehabilitation for all the four types PEM. Of the four types, only kwashiorkor with mean serum iron values of 15.6+1.51 micrograms/100ml and 21.17$\pm$ 0.33 micrgrams/100ml on admission and after rehabilitation respectively was significantly different. ($P<0.05$)

We recommended after the study to the authorities of OAUTHC that more attention should be paid to the management, feeding and diet given to these children to ensure greater and more rapid improvement in their rehabilitation (Alemnji, Thomas, Durosinmi, Taiwo Fakunle, 1995).

It has been also estimated that at least 40 million pre-school children are vitamin A deficient of whom at least 13 million (33%) already have some eye damage. The number of preschool children actually at risk of vitamin A deficiency with its consequences including blindness, reduced immunity and increased morbidity and mortality, is estimated at 190 millions. The majority of vitamin A deficient populations are found in 37 countries half of which are in the continent of Africa (UNICEF 1992). Nigeria is listed by the World Health organization (WHO) as a category one country having the highest risk of vitamin A deficiency (Humphrey, et al, 1992).

Reports from India (Gopaldes, *et al* 1993), Senegal (Calier, *et al*, 1991) and Nigeria (Adelekan, *et al* 1991) have documented vitamin A deficiency co-existing with malnutrition in pre-school children. At Ife, we investigated the nutritional and vitamin A

status of a group of preschool children whose habitual diet is high in carotene in Osu and Ibodi of Atakumosa Local Government area of Osun State, Southwest Nigeria. Our findings show that Dietary vitamin A intake appeared to be adequate in malnourished children and we concluded that childhood malnutrition of public health magnitude can co-exist with adequate dietary vitamin A intake or vitamin A status (Adelekan, Fatusi, Fakunle, Olotu, C.T. Olukoga, Jinadu, and Ojofeitimi, (1997).

(e) Pregnancy-induced Hypertension

Biochemical methods were used to monitor hypertension in pregnancy in our effort to aid the physicians in the intelligent monitoring and management of their patients.

Almost 10% of all pregnancies are affected by high blood pressure and the incidence is high if the woman is primigravidae or carrying multiple foetus (Thomas *et al* 1997). Several studies have shown that Nigerian women have comparatively lower blood pressure than their Caucasian counterpart both in the pregnant and non-pregnant states (Akinkugbe, 1973; Roberts, 1975), however Nigerian women have been shown to have a higher incidence of gestational hypertension (Okonofua, *et. al.,* 1992). Several metabolites such as uric acid, creatinine and total protein (Natrajan, *et. al., 1981)* and thyroid hormones (Rapin, *et. Al,* 1976), have been used to monitor hypertension in pregnancy with varying degree of success. Although there seems to be agreement about the increase of plasma thyroxine (T4) with stages of pregnancy, there are conflicting reports about the plasma levels of Thyrothrophin (TSH) and Tri-iodothyronine (T3) in both normotensive and hypertensive pregnancy. Our group therefore decided to estimate plasma T4, TSH and T3 levels in hypertensive pregnant women between the ages of 20 and 30 years in the second and third trimesters, and five days post partum.

Our findings on the plasma (TSH), (T4) and T3 levels in hypertensive pregnant Nigerian women revealed that second

trimester value for T4 was significantly lower ($P<0.05$) than the third trimester value for the normotive and hypertensive women; also the hypertensive women have a significantly higher ($P < 0.05$) T4 levels than their normotensive counterparts in the second and third trimester respectively. Our conclusion was that plasma T4 may be a good marker for monitoring hypertension in pregnancy (Thomas, Asaolu, Fakunle and Dare, 1997).

We also measured levels of some antioxidants in pregnancy with a view to investigating their role in the etiology of pregnancy-induced hypertension. The results showed that uric acid concentration was significantly higher and concentrations of catalase, Vitamin C were significantly lower ($P<0.01$) in the hypertensive pregnant women when compared with normotensive pregnant women in the second and third trimesters and in the post-partum period. We concluded that pregnancy per se reduced the concentration of the antioxidants but only the concentrations of Vitamin C were higher in late pregnancy in normotensive pregnant women. It was therefore suggested that high levels if Vitamin C may protect against pregnancy-induced hypertension (Tafie, 2006).

(f) Human Immunodeficiency Virus (HIV)/Acquired Immuno-deficiency Syndrome (AIDS) Research at Ife.

Human immunodeficiency virus (HIV) was first reported in 1983 at the Pasteur Institute in France (Barre-Sgompisso *et al* 1983). The first case in Nigeria was reported in 1986. Human deficiency virus infection/Acquired immunodeficiency syndrome (AIDS) is caused by two groups of cytopathic virus: HIV-1 and HIV-2. Human Immunodeficiency Virus-1 causes most HIV disease world-wide, while HIV-2 is confined to West Africa and its infection progresses more slowly than the HIV-1 (William 2004, Wiley *et al* 2003). Human immunodeficiency is a pandemic that has affected different regions, countries and populations in different ways and has become the focus of global concern. It attacks and destroys the immune system making it difficult for the body to fight infections

and diseases (Pace and leaf, 1997). It is transmitted predominantly by sexual intercourse, blood and blood products, sharing of infected needles or piercing objects or through transfusion. Mother to child transmission (MTCT) during pregnancy, childbirth or breast feeding has also been reported to account for about 25% of infection (Coovadia, 2004).

Free radical induced damage is suspected to be one of the mechanisms of the pathology of HIV disease and levels of antioxidants have been shown to fall below normal even before the development of AIDS with corresponding elevated levels of lipid peroxidation (Alland, et al. 1998). Antioxidant therapy with micronutrient such as selenium, zinc and vitamins C, E and beta – carotene has been shown to decrease HIV production and cellular oxidative stress. This correlates with improved CD4 count and reduction in viral load (Delanghe *et. al* 1998). Since information concerning antioxidant status and iron levels and their relationship to the severity of HIV infection and AIDS in Nigerian patients are scanty, we therefore decided to investigate serum iron level and some antioxidant micros-nutrients in HIV infected patients attending (OAUTHC), Ile-Ife.

Our findings showed that serum iron was elevated well above the normal values and antioxidant micronutrients were deficient in HIV infection. The low levels of the antioxidants support the use of micronutrients as adjuncts to therapy and that HIV – infected patients may benefit from antioxidant therapy (Oseni 2008).

RECOMMENDATION

LET NUTRITION BE YOUR MEDICINE

We all eat food and infact, our daily activities are to ensure that we have available food that is good to eat. Ignorance of the role of food in our lives causes much suffering and sorrow to the general population. The increasing interest in, and concern for the relationship between diet, nutrition, food habits and diseases of

lifestyle such as heart diseases, hypertension, stroke, cancer, diabetes, osteoporosis, arthritis, obesity and the like is global.

I have always had a strong passion for the science of nutrition which is an important aspect of Biochemistry. My doctoral work was on diet, nutrition and cancer. I have always believed, maybe because of my training that if there is any science that should be of interest to anyone, it should be nutritional sciences because of its immense benefits to man.

In the early 19th century, less than 10 percent of the world population died of heart diseases and stroke (and much of that was rheumatic heart disease). Today, it is more than 45 percent. At that time, less than 6 percent of the population died of cancer, and the figure is exceeding 25 percent today.

We are not meant to die in such numbers from heart attacks, strokes, diabetes and from cancer of the lungs, breast, prostate and colon. Significant cardiovascular disease began to emerge in the world especially in the Western World after World War I. It became rampant after World War II when people could afford diets rich in animal products and when the food industries began producing highly processed foods crammed with calories.

Also at this period (around 1900), most people got 70% of their protein from plant foods. Today, we get 70% of our protein from animal products, that are high in fat and cholesterol. Besides, animal products (foods) are usually eaten at the expense of complex-carbohydrate-rich foods such as grains, legumes, and vegetables. The average risk of heart disease of a man eating meat, eggs and dairy products is 45 percent. The risk for a man who leaves off meat is 15 percent. However the coronary risk of a vegetarian who leaves off meat, eggs and dairy products drops to 4 percent.

An editorial in the Journal of American Medical Association commended on these advantages. According to the editorial, a total

vegetarian diet can prevent up to 90% of our strokes and 97 percent of our heart attacks. Beyond this, it has also been proved beyond doubt that a very-low –fat vegetarian diet could reverse heart disease in patients scheduled for Coronary-by pass surgery. The risk of cancer of the prostate, breast and colon is three times, higher for people who consume meat, eggs and dairy products on a daily basis when compared to those who eat them sparingly or not all (Ludington and Diehll, 2000).

Mr. Vice-Chancellor, I would like to quote from the Holy Bible at this point. In Genesis 1:29, God said, *"I give you every seed bearing plant on the face of the whole earth and every tree that has fruit with the seed in it. They will be yours for food"* Also, in Genesis 2:8 & 9 *"Now the Lord God had planted a garden in the east, in Eden; and there he put the (man and woman) he had formed. And the Lord God made all kinds of trees grow out of the ground – trees that were pleasing to the eye and good for food"*. From the two Bible passages I have cited, I am convinced that our God, the Creator avoided prescribing animal products for diet for a purpose, may be to avoid these killer diseases, for a better healthy living so that our days may be long.

Mr. Vice-Chancellor, to win the battle against the epidemic of western lifestyle diseases, we must let nutrition be our medicine and break away from the lethal excesses of today's western diet. We need a simpler, more natural way to eat. Our diets should consist of a wide variety of foods (whole grains, tuber and legumes, fruits and vegetables) simply prepared with sparing use of fats and oils, sugars and salt and of course plenty of water. We may use refined products and animal products only sparingly. This is the type of diet that can prevent most of these killer diseases and probably reverse them.

CONCLUDING REMARKS

The study of Human Biochemistry has opened our eyes to how the body works as a chemical system. From a physician's point of view, Biochemistry not only describes how the system works, but also provides a foundation for understanding how to improve its operation (e.g. by appropriate nutrition and exercise) how to diagnose problems, and, if possible, how to remedy them.

One of the physicians' most important skilis is the ability to apply basic science to a clinical setting. To develop this skill, Medical Biochemistry combines chemical, physiological and pathological perspectives of Human Biochemistry. I have throughout my academic career especially at Obafemi Awolowo University taught Biochemistry to Nursing, Medical Rehabilitation, dental and medical students; I have also taught postgraduate students as well and collaborated with colleagues within and outside the College of Health Sciences in research efforts with relevance and pertinence to the promotion of the health of man and also developed an understanding of Biochemistry as an everyday science, a science that is useful in the laboratory as in the hospital ward or the physician's office.

Aside from performing research to improve the health of Nigerians, I also contributed in the area of the University administration, service and manpower needs of the country. I served as the Head of Department of Chemical Pathology for thirteen (13) years, Vice-Dean and Dean of the my Faculty in addition to serving at various committees at the Departmental, the Faculty and University levels. Outside of the University, I served as a resource person at the National level especially at the Federal Ministry of Environment. I was appointed as a member of Council of Bayero University, Kano by the Federal Government and I served in the Council of the University for four (4) years.

In the area of manpower development our Postgraduate programme started in real earnest in 1985 when I joined the University and

since then the learning and training of Biochemistry has developed by leaps and bounds.

Our Department has made enormous contributions in the areas of clinical and nutritional Biochemistry. The hallmark of the research contribution initiated and implemented in the Department is its relevance and pertinence to the promotion of health of Nigerians. The highlights are impressive and these findings have been documented in highly reputed scientific journals.

The Department has produced 7 Masters and 5 doctoral graduates. The current Head of Department of Medical Biochemistry Dr. (Mrs) B. O. Emma-Okon obtained her doctoral degree in the Department under my supervision. During her training she had the opportunity of working with experts in Human Reproductive Unit, Medical Council, Edinburgh in the United Kingdom for the study of prostaglandins. Dr. O. O Oyelola obtained his Ph.D. degree in the Department in 1990. He later proceeded to Case Western Reserve University, Ohio in the United States of America as a post-doctoral fellow. He is currently resident in the U.S.A. as a professor in one of the Universities. Dr. I. O. Ogunleye (now Oluwaleye) also obtained his doctoral degree the same year; taught in several Universities in this country. Dr. Alemnji, a foreign student also had his postgraduate training in the Department. He is also in the U.S.A. as a University teacher. Professor (Mrs) M. F. Asaolu, also trained in the Department, is the current Head of the Department of Biochemistry, Ekiti State University, Ado-Ekiti.

Our products have been exposed to top-notch and world class laboratories for their training and have always met international standards. By and large, the Department has produced considerable manpower for leadership in Nigeria and global community.

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