Then and Now:
Unravelling the Mysteries of Ill Health through Research

Lateef Salako, NNOM
Director-General
Nigerian Institute of Medical Research, Yaba, Lagos

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c/o Professor Mrs. O. Osuntokun
University of Ibadan
U.I. P.O. Box 93881
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It is an honour for me to be invited to give this lecture, the first in its series, in memory of a colleague who would rank comfortably as one of the most intellectually exciting medical scientists of our times. Nevertheless, I would have been happier if this event had not been necessary. But who are we to question or dispute the way the Almighty giver and taker of life has decreed the order in which His creations will come and go? So, when these sad things happen, shattering though they are, we have no choice but to accept their inevitability, learn to live with and make the best out of them.

Although this is the first in the series of the Benjamin Oluwakayode Osuntokun Memorial Lectures by the Benjamin Oluwakayode Osuntokun Memorial Trust, it is not the first lecture in memory of Kayode. The Global Advisory Committee on Health Research in which Kayode Osuntokun served for several years as Chairman and member, in recognition of the excellence with which he served the committee, took the unusual step of organising a lecture in his memory at a conference in Geneva. This was delivered on behalf of the Committee by Adetokunbo Lucas on 16 October 1996, in recognition of the unsurpassed excellence with which this most distinguished health scientist served humanity.

In preparing my own lecture, I had the advantage of talking with Tokunbo Lucas about his lecture, as well as reading the full

text of that lecture.[1] This, of course, was not the only work I consulted in preparing this lecture, nor was it the most important. It was indeed a great intellectual feast for me to go back and re-read some of the works that established Osuntokun as a great health researcher. Among them, I particularly enjoyed reading his monumental PhD thesis on Tropical Neuropathy,[2] his MD thesis on the pathophysiology of peripheral nerve damage in Nigerian diabetics[3] and several prize-winning journal publications.[4-10] Although I was already familiar with these studies, re-reading them gave me a new appreciation of the magnitude and excellence of his contribution to knowledge in every subject he studied.

I recognise that it would be most unusual in a lecture like this for the lecturer to skip altogether reflections on the subject's life, and I am too conventional to do the unusual. Though a good amount has been written about Kayode Osuntokun's life in the past two years, he lived such a full and eventful life that it is possible to recall aspects of his life with no danger of being repetitious. So, I shall start my lecture with some personal reflections on our departed colleague before going on to the primary subject of this lecture.

My first contact with Osuntokun was precisely on the evening of Wednesday, 29 September 1954, when the incoming freshmen at the University College Ibadan — about 145 of us — gathered together for dinner at Mellanby Hall. There, by a strange twist of fate, three of us who had travelled by train from Lagos that day (Jide Smith, Siji Osunkoya and myself) met a group of Christ's School, Ado-Ekiti old boys through the good offices of Ayo Olatunde, who worked in the same laboratory

with Smith and Osunkoya. From this inauspicious meeting began a life-long association of intellectually rewarding comradeship.

Many who have written on Kayode's life at the University College, Ibadan have dwelt almost entirely on his exploits and achievements in the academic field. These accounts, however, ignore the fact that Ibadan, in the 1950s and early 60s, was as much a centre of culture as a centre of learning. Osuntokun readily availed himself of all the opportunities open to an adventurous young man in such a milieu. Hence, his academic achievements represent only one aspect of his many activities.

He was a member of practically every social club in the institution and he participated actively in all socio-cultural activities. He rarely missed a drama, film show, opera, musical recital or dance — all of which took place regularly in the University at that time. Even a major university examination scheduled for the following day could not keep him away. Often, he would return from a cultural event at 12.00 midnight and still work at his books until 6 a.m., effortlessly. He seemed to have an enormous capacity for work and play that most ordinary mortals do not possess. A keen sportsman, Osuntokun represented the University in lawn tennis and his halls of residence (Kuti Hall and the Clinical Student's Hostel) in table tennis and football. His exploits on the football field bring back pleasant memories of 'Orlando' (as he was fondly called) to those who knew him during his Christ's School days. On the lawn tennis court of UCI, he was the one person the lecturers wanted to meet and beat. They succeeded in meeting him, but rarely had the satisfaction of beating him!

Osuntokun also made remarkable contributions to many organisations. One on which he left an enduring mark is the Association of Medical Students of Nigeria. He served as secretary of the association for three years and what a secretary! In fact, he performed not only the duties of secretary, but also practically those of president and even treasurer. I should know, because I was the treasurer during this time. On his own, he took on the tasks of soliciting for funds, banking and keeping the books. I was only called upon to sign for withdrawal of funds or to accompany him on some of his fund-raising visits. Such was the application, dedication and commitment he brought to everything he did: everything had to be done to perfection.

Generously talented in various fields, it was impossible for one to undertake a serious discussion with Osuntokun on any topic without learning something. Personally, I have been infinitely better informed and made more worldly-wise by my interaction with him. One of such occasions served me so well that I gladly recount it. In 1976, Osuntokun, two other colleagues and I, undertook a tour of the American Schools of Osteopathic Medicine on behalf of the Nigerian Medical Council. The purpose of this tour was for the Nigerian Medical Council to study Osteopathic Education in the United States of America, and make recommendations to the Nigerian Medical Council on the advisability of registering osteopaths for practice in Nigeria. We agreed at the beginning of our assignment that I would write the report, and it took me about a month to complete it. This was not soon enough for Osuntokun. He clearly did not approve the report taking such a long time, but he did not say anything about it. Instead, he looked for an opportunity to show me that

it could be done within a much shorter period. He did not have to wait long. The following year, he and I undertook a tour of American Medical Schools, on behalf of the University of Ibadan, to explore possibilities of teaching and research collaboration in the basic medical sciences. This time, he was to write the report.

Our trip, which took us through the length and breadth of the United States, was completed in three weeks and we headed for home. We were only a few minutes into our flight home when Osuntokun opened his briefcase and handed me a neatly-typed ninety-page document. That was my copy of the agreed report. How did he achieve such a feat? Every night at dinner, after our day's work, we discussed the day's issues and agreed upon our report. He then went to his room, wrote it out, and gave it to our next host for his secretary to type the following morning. In this way, the entire report was written, typed, and ready to be delivered by the time we finished our mission. This lesson sank in deeply and I used it to good advantage years later when I served as chairman of several national and international expert committees. After studying the background papers and the agenda, I would prepare a draft report even before the meeting started and amend it as the meeting went on so that the final report was ready for adoption before the participants dispersed.

So much for my reflections on some of the exciting times shared with Osuntokun over the past forty years. Now to the real subject of my lecture. In choosing the title, *Then and Now: Unravelling the mystery of ill health through research*, I deliberately decided to focus on one specific area of health discipline to which Osuntokun directed boundless energy. As

some of us know, he was as outstanding in health research as in clinical practice, medical education, health policy development and in management. I have chosen to speak on health research because it is an area that I feel most comfortable commenting about, and not necessarily the one in which he made his most enduring contribution. In discussing the subject, I shall briefly explain the concept of health research and its role in the development of health care practice. I shall, using a few of the diseases that have been investigated by Osuntokun, his contemporaries and other scientists in this country, illustrate how quality research can modulate our views of the diseases that afflict us, and lead to a better understanding of their causation, and the development of interventions and tools for community control and individual treatment.

. *Then and now*: how far back is my 'then'? It goes as far back as forty years ago, when Osuntokun entered the health scene, and occasionally beyond that; and 'now' is the present time. How has research altered our understanding and handling of diseases and health problems in general? This will be the focus of the lecture.

Research, Scientific Research, Health Research and Essential National Health Research

At this stage, let me clarify my usage of the term *research* in the context of this lecture. Research is any activity that generates new knowledge and a better understanding of natural phenomena. Scientific research uses scientific methods to explore, hence discover new facts, and has the capacity to use the new knowledge to solve practical problems and explain

natural occurrences and phenomena. Health research, which is the type of research that concerns us in this lecture, is a:

> . . . process for obtaining systematic knowledge and technology which can be used for the improvement of the health of individuals or groups. It provides basic information on the state of health and disease of the population; it aims to develop tools to prevent and cure illness and mitigate its effects and it attempts to devise better approaches to health care for the individual and community.[11]

The coverage of health research ranges from basic observations in the natural sciences (basic research) to strategic and operational research focussed on well defined aspects of specific diseases. Health research also spans a wide variety of disciplines; from the precision of the physical sciences to the uncertainties of the behavioural and social sciences. No matter what the nature of the research is, it is governed by the same fundamental principles that govern all scientific enquiry, one of which is that measurements are made using adequate controls.

Progress in health care depends heavily upon health research, as will be shown later using examples from studies done in Nigeria. Every nation needs to conduct research on country-specific health problems to provide information on diseases. This information will, in turn, serve as the basis for counteractive measures. This is what is now called Essential National Health Research.[12] It shall become clear later in the lecture, how research by Osuntokun and others led to an understanding of

important diseases affecting Nigerians, and how this prompted the development of disease intervention and control.

Varieties of Health Research

Health research is heterogeneous, despite the common goal of increasing understanding which leads to improved control. Among the more important varieties of health research is what we now loosely call 'strategic research'.[13] The purpose of strategic research is primarily to increase the understanding of a significant health problem, in order to eventually solve the problem or reduce its impact. Strategic research encompasses many disciplines, reflecting the multifactorial origins and impacts of most health problems. In addition, health problems derive not only from conditions with a heavy disease burden, but also from inefficiencies and inadequacies in health systems. Accordingly, strategic health research activities are undertaken in the areas of the biomedical sciences (which include the biological, preclinical and clinical sciences), population sciences (which include epidemiology, demography and behavioural sciences), and health policy sciences (which include health policy research and health systems research which in turn includes health services research).

For any given health problem, contributions from different investigators in different disciplines complement one another, thereby collectively producing the desired solutions.

Another variety of health research is what has been broadly described, for want of a better term, as 'developmental research'. Whereas it is very easy to see how strategic research contributes to the generation of new knowledge and, therefore,

constitutes research, however one defines the term, it is sometimes held out that the generation of new knowledge is not necessarily an element of product development and so, is strictly not a research activity. It is now widely accepted, however, that development of new disease control tools involves problem solving activities, which include hypothesis generation, testing, and acceptance or rejection, which are hallmarks of research.

Developmental research, therefore, combines knowledge generation with the direct or immediate use of that knowledge to develop new products, interventions and policies or to improve old ones. The products include drugs, vaccines, diagnostics and equipment, and the interventions include health education, disease surveillance, algorithms of integrated diagnosis and management of the sick patient, and improved devices for storiage of drinking water and waste disposal. All these should lead to enhanced health promotion, disease prevention and disease management at individual and community levels. The policies include steps to obtain instruments for the prevention, treatment and control of diseases.

Developmental research is particularly directed towards:

- evaluation of new products, interventions and policies for disease control;
- evaluation of control programmes; and
- studies on the socio-economic and behavioural factors affecting diseases.

Who Does Research and Where?

There has always been a myth about research to the extent that many consider it the preserve of a few scientists in institutions specially designed for such 'esoteric' pursuits. This is probably encouraged by established researchers themselves, partly to make them feel superior to their non-researching colleagues. This picture of health research is totally mistaken. Far from being the preserve of a few reclusive overqualified individuals, health research can be undertaken by anyone capable of collecting new information. Thus, a primary health care worker or rural medical officer can undertake health research similar to that of a professor with the most high-sounding academic degrees and professional diplomas; and the research can be pursued as much in the field as in a clinic or laboratory that is equipped with the most sophisticated high technology equipment.

With these general remarks on research as a background, I can now go on to describe a few examples of how research has helped to: (i) identify our health problems, (ii) assess the impact of the health problems on the health and economic development of the people, and (iii) develop effective strategies for solving the identified problems. I have no apologies for beginning this scientific exploration with the first disease to attract Osuntokun's attention and which made him the great scientific investigator that he became — that is, tropical neuropathy.

Tropical Neuropathy (TN)

Anyone who worked in the University College Hospital Ibadan, Nigeria in the first few years of its existence, (to be specific, in the 1950s and 60s), would be very familiar with this condition. Characterised by peripheral polyneuropathy with ataxic gait,

paraesthesiae and dysaesthesiae in the distal parts of the limbs, impaired hearing and vision and stomatoglossitis, it was responsible for up to 25 per cent of neurology in-patients at that time,[14] and was a common sight at the medical out-patients. It is one of the marvels of medicine and a great tribute to health research that this condition is hardly ever seen these days.

The earliest description of this disease in Nigeria was made in the late 1920s and early 30s. Under a variety of titles, Dr. D. G. Fitzgerald Moore — a medical officer in the colonial medical service in Nigeria — described a syndrome characterised by impaired vision and preceded or associated with a sore tongue and mouth, indicative of avitaminosis B[15-19] in a series of articles in the *West African Medical Journal* between 1930 and 1935. Dietary investigation led him to postulate the cause of the syndrome as either a dietary toxin or a dietary deficiency, in both cases associated with the almost exclusive consumption of gari as the staple food. Moore rested the case for a dietary toxin on the evidence that a single foodstuff seemed to be responsible for the condition. He reasoned that this could not be simple carbohydrate excess, because in places where gari was not consumed so exclusively, the disease was not seen even if the diet was still mainly carbohydrate. In favour of a dietary deficiency cause — specifically vitamin B — was the evidence that in early cases, dietary supplementation with vitamin B-rich preparations produced a cure, although this was not always so in late and severe cases.

On the strength of nothing more than the foregoing analysis, Moore concluded that 'this cannot be accepted entirely on present evidence'. He subsequently went on to suggest that 'there

is much research work to be done in this particular deficiency because it is a definite common and simple disease'. In the description of this disease in the 1930s, one noticed, with only very few exceptions, the absence of any mention of peripheral neuropathy.[20,21] It would be unlikely that none of the patients encountered in those days manifested any peripheral neurological features. It is more likely that these features escaped notice because the reporting doctors lacked the skills for detailed neurological assessment.

The call by Moore for further studies into the causation of this disease was not taken up to any great extent until Osuntokun's work in the 1960s and 70s which followed close on the heels of the reopening of interest in the condition by another legend of Nigerian medicine — G.L. Monekosso.[22-25] Osuntokun's studies on this disease were remarkable not only in the depth of their coverage, but also in the extent. He produced the most comprehensive clinical description of the syndrome and then went on to study its epidemiology, its biochemistry and histopathology, its pathophysiology and aetiology, and finally its treatment.

Early in his studies of the disease, he had eliminated, as a result of clinical and epidemiological findings, the possibility that vitamin B deficiency was the sole or major cause of the disease. This led him to focus on the role of dietary toxins as the main cause. The interval between the studies by Moore in the 1930s and those of the 1960s facilitated the observations that peripheral polyneuropathy of nutritional origin mimicked chronic cyanide intoxication observed in prisoner-of-war camps during the Second World War. A systematic study of cyanide metabolism

in the patients with tropical neuropathy gave findings that were consistent with that of chronic non-lethal exposure to cyanide in the amounts that were ingested with excessive consumption of cassava in the form of gari. The conclusive demonstration of gari and cyanide as the cause of tropical neuropathy had obvious implications for therapeutic intervention and prevention. The need to include other food items in a normal diet was a logical therapeutic and preventive approach that followed directly from the findings, and its adoption has proved very successful. Cyanide is toxic to the enzymes responsible for carbohydrate metabolism in the nervous tissue and the presence of other food items apart from gari in a normal diet would supply compounds, which in modern terminology, would provide antioxidants that would counteract the effect of cyanide in gari.[26] There should, therefore, be no fear of taking gari as long as it is taken in moderation and not exclusively.

One would be tempted to say that as far back as the early years of this medical school, the studies by Osuntokun on tropical neuropathy set the pattern on which future research on our health problems would be modelled. I do not know any other disease in this country that has been investigated to such an extent with such incisive scholarship and painstaking thoroughness.

Child Health Care

The seed of child health care in Nigeria was sown in Lagos in 1925 with the first appointment — by the Colony of Lagos Health Authorities — of three health visitors charged with the responsibility of visiting the homes of recently delivered mothers

to urge them to take their babies to government dispensaries or to properly qualified doctors for good medical care. This was followed by the establishment of the first infant welfare clinic in Lagos in 1928, with emphasis on educating mothers on preventive medical actions.[27] The ground was thus prepared for the accurate recording of trends in childhood morbidity and mortality, the harvest of which would be the development of rational approaches to child-care based on new knowledge and understanding of childhood illnesses obtained from these records.

In 1929, the infant mortality rate in Lagos was 134 per thousand live births with 45.3% of the deaths occurring in the first four weeks of life. The four commonest causes of death were respiratory tract infections 14%, convulsions 10%, malaria 5.9% and diarrhoea 4.8%. In the second year of life, the child mortality rate was 35.5 per thousand births with the four commonest causes of death being again malaria 23.5%, diarrhoea 21.9%, convulsions 16.2% and respiratory tract infections 15.4%. It is immediately obvious that three of the main causes of childhood deaths about 70 years ago are still the main causes today, and that with an estimated infant mortality rate of 84 per thousand live births for the whole country in 1997, we have only managed to reduce the infant mortality rate years by less than 50%.

This, however, does not constitute the theme of my discussion. What I want to direct attention to here is the number of deaths from the condition vaguely called 'convulsions' which was responsible for 10% of deaths in the first year and 16.2% in the second year. In the 1920s and 30s, this condition was not explained beyond the statement that it excluded explicit diagnoses

like bronchopneumonia, malaria, enteritis, and other common childhood diseases.[28] Following these early observations, the problem of convulsions — a nagging one at that — and its contribution to childhood morbidity and mortality has continued to engage the attention of medical personnel through the decades up to the present time. The major breakthrough in diagnosis and management was, however, not made until the specialised paediatric services of this hospital and the Wesley Guild Hospital, Ilesa, Nigeria, came into being in the 1950s.

In the 1960s, a fresh reexamination of the problem brought out some new facts which have led to some health education interventions on how to manage convulsions and the high fever that is usually associated with it, both in the health facility and at home. Studies associating high mortality from childhood febrile convulsions with home treatment using a particularly toxic decoction based on cow's urine were published in Ibadan in the 1970s.[29] Several authors confirmed the high frequency of occurrence of febrile convulsions in Nigerian children aged 6 months to five years, and confirmed a higher mortality from the disturbance than was reported elsewhere. Of far-reaching importance was the finding that home treatment of the convulsing child with a local concoction based on cow's urine was associated with higher frequency of hypoglycaemia and mortality in the patients. Later studies also incriminated hypoglycaemia and repeated convulsions as risk factors for increased mortality in febrile convulsions occurring in the course of diseases like cerebral malaria.[30]

These studies had immediate practical applications. For example, the association of convulsions with malaria in almost

50% of cases in one study was a sound rationale for the administration of antimalarials to febrile convulsing children when it is not possible to do the diagnostic test to eliminate malaria immediately. Administration of an anticonvulsant to a child who has had a convulsion, to prevent further convulsions, or even to one who has not yet had a convulsion, but has an infection like malaria with hyperpyrexia is now widely accepted. It is also an effective therapeutic and prophylactic practice as much as is the administration of a bolus dose of glucose to correct or prevent hypoglycaemia especially in situations where blood sugar analysis is not immediately possible.

Finally, these studies, by firmly incriminating the local cow's urine concoction in the increased mortality in childhood convulsion, identified a target for community health education — the widespread adoption of which has resulted in a dramatic reduction in severe morbidity and prevention of avoidable mortality from febrile convulsions.

Yellow Fever

Yellow fever is the junior partner of the pair of dreaded diseases (the senior partner being malaria) that made West Africa so inhospitable to European colonisers, that they found it impossible to occupy and seize the land for their own use as they did with devastating consequences in South Africa, and to a lesser extent, in East Africa.

Yellow fever has probably afflicted the inhabitants of West Africa, indigenes and visitors alike, for centuries, but the story of its recognition and conquest can be made to fit into this century.[30] Its elimination started with the appointment by the

British Government of a Yellow Fever Commission, following a series of high mortality epidemics characterised by fever, jaundice and haemorrhages that occurred in West Africa in 1910-11. The commission confirmed these and previous similar epidemics in the same area to be due to yellow fever and made recommendations which prepared the ground for the dramatic events of 1926 and beyond. When the Rockefeller Foundation started its programme on the 'Great Neglected Diseases of the World' in the 1920s, it was predictable that yellow fever would be one of the neglected diseases that would attract its attention, given the loss of lives that was still occurring from the disease in the Caribbean and in Central America. The Rockefeller Foundation thus established a Yellow Fever Commission within its International Health Board.

When another yellow fever epidemic occurred in West Africa in 1926, it provided an opportunity for the Commission to send an international research team to Lagos to undertake a comprehensive investigation of the disease. This task started with the building of a yellow fever research station in Lagos with a branch in Accra. There, leading authorities in yellow fever research laboured relentlessly to solve the problem of this age-old scourge. The international team of scientists engaged in the yellow fever research in Lagos at that time included: Professor Adrian Stokes from Guy's Hospital Medical School in London; and Dr. Hideyo Noguchi, a Japanese American from the Rockefeller University in New York who had worked on the disease in the Caribbean and in Panama and who firmly believed that yellow fever was caused by a spirochaete and not a virus.

This concerted international endeavour finally established the viral cause of yellow fever beyond doubt.

A great deal of progress was made in this same year (1926) when a Ghanaian labourer called Asibi, working at the Yellow Fever Research Station in Yaba, contracted the disease and, fortunately for him, recovered. Blood collected from him during his illness was inoculated into a rhesus monkey which became infected, and the infection could be passaged serially through several monkeys. In this way, the Asibi strain of the yellow fever virus was established. It was subsequently found that white mice were susceptible to yellow fever and that the Asibi strain of the virus could be successfully passaged serially in the brain of mice. The attenuated virus obtained in this way provided the first product for an effective vaccination against the disease which was widely used to good effect in the early 1930s, even if by modern standards the vaccine would be regarded as rather crude. Nevertheless, the investigators did not rest on their oars. They continued in their efforts to improve the vaccine. The next big success in this effort was the discovery that the virus could be grown in chick embryo. The use of this technique led to a profound modification in the virus itself, so much so that the vaccine produced by this method was safer and more effective than the vaccine produced from the Asibi strain. The strain of virus produced by growing it in chick embryo is the famous 17D strain which is still used in the production of yellow fever vaccine till today.

Unfortunately, the remarkable story of the conquest of yellow fever did not have a happy ending for some of its most distinguished dramatis personae and is probably why no Nobel

Prize came out of the work. Professor Adrian Stokes was the first victim in 1927.[31] He was said to have performed a post mortem examination on an Asibi strain infected monkey without using gloves, which was not unusual in those days. However, because he had a cut on his hand, he developed yellow fever and died. Next was Noguchi. He was still sceptical about a virus rather than a spirochaete being the cause of yellow fever, even after the isolation of the virus from Asibi. He was thought by his contemporaries to have inoculated himself with infected material either to disprove the virus theory or to perform harakiri following Stoke's death. Needless to say, he got yellow fever and died in 1928. The young pathologist, William Alexander Young, who performed the post mortem on Noguchi died of the disease within three weeks.[32] So, that was the price the world paid for the ground-breaking discovery of the cause of yellow fever and the development of the first effective vaccines against the disease. What did we do with the discoveries? — one may be tempted to ask.

The advantage to the Europeans was immediate. The availability of a reasonably safe and effective yellow fever vaccine meant that they had relief from one of the two principal scourges, yellow fever and malaria, that had made the West African region so inhospitable to them. All they needed to do, subsequently, was to concentrate efforts on finding a similar solution to the malaria problem to enable them put in place definitive plans for the occupation of the territories they had already annexed. Unfortunately for them, but fortunately for us, the conquest of malaria proved an infinitely harder task than that of yellow fever, hence their occupation plans could not

materialise before the independence movements of the 1940s and 50s finally forced them out of the region.

How did this benefit the local populace? The yellow fever story must be the first example of a now very known fact that getting an effective disease control tool does not necessarily herald the impending eradication of the disease. It is one thing to have the tool, be it a medicine or a vaccine, it is another to get it to the people who need it. It is a sad reflection of the state of our health care policy and actions that up till now, we have not been able to solve the problem of the procurement and distribution of the vaccine for yellow fever. Consequently, almost 70 years after the development of an effective vaccine for it in our country, we still have to contend with the usual 10-year cycles of yellow fever epidemics.

I think it would be unkind to all concerned to say that the situation above arises because we neither care nor try. Having served in government and close to policy makers, I know that in respect of this particular disease, we did try. Following the last national outbreak of yellow fever about 10 years ago and the difficulty experienced in procuring vaccines from abroad, a decision was taken to transfer back to the country the technology for producing yellow fever vaccine. Accordingly, a huge sum of money was spent on establishing a yellow fever vaccine production laboratory and procuring equipment, materials and supplies for the vaccine production. Training and collaboration agreements were also entered into with foreign partners. The ultramodern vaccine production laboratory was duly opened in 1992, but within a few weeks of that event, there was a change of state ministers. The laboratory has remained idle since.

Surely, this lack of sustainability of effort must be one of the major factors bedevilling our health care programmes: it is an area calling for serious study. Fortunately, this kind of failure is not peculiar to Nigeria, and it is the widespread recognition of the need to do something about it that has stimulated interest in the promotion of health systems research or health management research worldwide.

Hypertension and Cardiovascular Diseases

One of the most striking observations when reading Nigerian and even West African Medical literature up to the beginning of the Second World War is the almost total absence of any reference whatsoever to hypertension or even other cardiovascular diseases. There are no reports of heart failure and hardly any of rheumatic heart disease, stroke or renal disease. Not only would you not come across a hypertensive disease being referred to as a disease on its own, you will not even find a report of the blood pressure record of any patient in the literature. Equally, you scarcely find records of findings on examination of the heart, e.g., auscultatory heart sounds. In preparing for this lecture, I read every article published in the old series of the *West African Medical Journal* — a publication which commenced at the beginning of 1927 and went out of circulation at the end of 1938 — and not once did I see a record of blood pressure measurement for African or European patients in Nigeria during that period. Little wonder that contemporary writers claim that hypertension was unknown in the African until during and after the Second World War. Is it not logical, considering the evidence before us, to deduce that physicians working in Africa

before the Second World War did not include the sphygmomanometer in their diagnostic kit and so could not have known whether hypertension existed or not? We know from records elsewhere that hypertension was found regularly in Europeans in other parts of the world, yet it was never reported in any European in Nigeria during that period.

The lesson is clear, you cannot detect hypertension if you do not measure blood pressure. The physicians of those days could not claim ignorance of hypertension or how to measure blood pressure. The sphygmomanometer was introduced into medical practice in 1896 and had proved a simple and reliable device for measuring blood pressure. What is more, the international medical literature of the 1930s was replete with reports and debates on the usefulness of the then only effective method of lowering raised arterial blood pressure — a radical and mutilating surgical procedure termed lumbo-sacral sympathectomy. Hypertension must, therefore, have existed in Nigerians in those days, but it escaped notice because no one cared to measure the blood pressure.

The modern era of hypertension research in Nigeria undoubtedly coincided with the establishment, in the early 1950s, of the medical faculty of the University College Ibadan which functioned from the Adeoyo Hospital, Ibadan before the University College Hospital was opened in 1957. The first epidemiological surveys of hypertension and hypertensive diseases in Nigeria were carrried out in 1960,[33, 34] although individual cases had been seen, studied and treated at the University College Hospital for some years before then.[14] Admissions for hypertension and out-patient records in the 1950s

and 60s showed, for the first time that, far from being non-existent in Nigerians, hypertension was in fact one of the commonest non-communicable diseases in the country and was responsible for a good number of cases of heart failure, renal failure and stroke. This new finding led to a complete swing in the pendulum of opinion from what was once claimed to be non-existent to what was then considered (from insufficient clinical and epidemiological evidence) I dare say, more common in Africans than in other races, and found to occur at a lower age, and pursued a more rapid fatal course.

This last view (that is, that hypertension in Africans was more rapidly progressive than in white races) stemmed from the fact that a high percentage of the patients seen in those days had severe and often complicated forms of the disease, with death occurring from heart failure or malignant hypertension within a short time of the patient's first visit to the hospital. With the benefit of hindsight, it should have been obvious to us that the severe hypertensives seen in those days were selected hospital patients and did not represent the general population pattern. It should also have been clear that the severe cases seen in hospitals in the 1950s, when sphygmomanometers became adopted for use, were the mild cases that were not detected 10-20 years previously and had, in the interval, progressed steadily to the severe form of the disease which was soon to take their lives.

The earliest attempts to correct the omissions of the past and obtain a reasonable idea of the extent of the public health problem posed by hypertension and hypertensive diseases were made by physicians of the Department of Medicine of UCH in

the late 1950s, and this tradition has continued in that department ever since. Their research which covered the epidemiology, clinical features, prognosis, risk factors, aetiology, pathogenesis and treatment of the condition has provided good understanding of hypertension and hypertensive diseases in this country; has led to the introduction of appropriate therapeutic approaches for the individual patient and recommendations for the community control of the disease. For a condition that is found in about 14% of the adult population and for which treatment is life-long, concentration of efforts on the treatment of individual patients means that only a small fraction of the affected population would be covered. For uncomplicated, mild and moderate hypertension in particular, the numbers requiring drug treatment are so large that it would be impossible to reach all of them even if the drugs were available and affordable, which is not the case. Non-pharmacological interventions which can be applied on community-wide basis, and would be effective enough to reduce the frequency of occurrence of the condition, and prevent its deadly complications are required. Recent government-sponsored studies which shed light on the risk factors of the disease[35] should go a long way in helping the health authorities design effective interventions for the control of hypertension in the population at large.

At the individual level, the researches referred to earlier have led to the development of treatment protocols for individual patients which if properly followed, should lead to adequate and satisfactory reduction of the raised blood pressure in the individual patient. The patient should thus be able to lead a normal life, that is not shortened by hypertension or any of its

dreaded complications. This is a far cry from the gloomy picture of the 1950s and 60s. Although hypertension is a global disease, it has racially peculiar characteristics. The appreciation of this peculiarity is important for the proper understanding of the disease in particular areas, and such understanding is indispensable for the development and institution of appropriate control measures. It is in this context that the studies of the disease, undertaken in this country in the past 30-40 years, have made the breakthroughs that have rendered the control of this disease, with all the associated social, economic, behavioural and biological peculiarities an achievable reality.

This completes the brief survey of some of the diseases which have been subjects of extensive investigation locally and for which, thanks to those investigations, new understanding has been generated that has been useful in developing interventions which are of great help in reducing the disease burdens on our people. There are countless numbers of these diseases. I have only chosen these four to illustrate, and not necessarily to give a comprehensive account of our contributions in this regard. It is one thing, however, to produce new knowledge about a disease — new knowledge that can be useful in solving the health problems caused by the disease — and it is another for the health authorities to use the new knowledge for the benefit of the masses. This takes me to the next aspect, that is, incorporating research findings into national health care policies and actions.

From Health Research to Health Policy and Action

Considering that health research is 'a process of obtaining systematic knowledge and technology which can be used for the

improvement of the health of individuals or groups',[30] it is important for health researchers not only to describe their research methodologies accurately, but also to be purposeful with regards to how their work will improve the health of the people. It also behoves health care authorities to be familiar with national health problems, to get involved with planned and on-going research aimed at generating new information, and to be ready to apply any new knowledge that is obtained to provide solutions to the existing problems.

In this country in the past, that is, before the establishment of the medical colleges and teaching hospitals, health research was undertaken mostly by personnel of the health department. The permission of the Director of Medical Services was sought and obtained before any research was embarked upon, and the findings were reported to a medical meeting or published in a medical journal. It is, therefore, not surprising that recommendations for control interventions emanating from research reports were often quickly adopted and implemented in health care actions. For example, from the early studies on tropical neuropathy which took place in the 1930s, the dietary recommendation for vitamin B supplementation was promptly adopted by government and directives were sent to all institutions under government control to implement it immediately. Unfortunately, the poor mass communication system in those days made public enlightenment and mass mobilization for desirable intervention almost impossible. Similarly, from the yellow fever studies came the commercial production of the yellow fever vaccine and its use for the prevention of yellow fever immediately after it was developed in the laboratory.

However, with the universities entering the health research scene, government control of health research came to an abrupt end. With that change also came the fact that research findings no longer had to be reported to the health authorities, thus leaving room for far-reaching findings to go unnoticed by the health authorities. Even when the findings are brought to the attention of the authorities, and the research is commissioned by them, there has been, over the years, a definite and deteriorating lack of commitment in translating such findings into action. This is not surprising given the distinct lack of political will to implement well-tested interventions that have been deliberately enshrined in the national health policy.

Intensive research is called for in the area of health policy and management to determine the factors that contribute to persistent failure to utilise research findings in health actions, and how these can be corrected. Many observers have, in the recent past, offered suggestions as to the causes of these failures. These, however, are mostly personal views and conjectures based on untested ideas rather than on properly evaluated scientific enquiries. The kind of research needed falls in the realm of health systems research which at the present time, is in its infancy everywhere, but is as important as the strategic and developmental research which I have explained earlier. I will, therefore, devote the concluding part of this lecture to a short discussion of this subject which, incidentally, was the area of research to which Osuntokun devoted his attention in his last years.

Health Systems and Health Policy Research

Health Systems Research is the broadcast form of health research since it covers the entire health programme of a country as opposed to other forms of health research which address, for the most part, specific health or disease problems. It can be undertaken at the micro level as when we study, for example, factors influencing bed occupancy or repeat out-patient hospital attendance at the UCH (which comes under health services research). It also addresses areas like national health policy options at the macro level, and what determines them. Examples of this are fees for service, cost recovery, health care financing in general, alternative medicine, essential drugs programme and so on. Health systems research techniques used belong to the social, economic and behavioural sciences and the results, in general, provide information which can be used to assess the effectiveness of the health system or systems in use in a country, the health policy and the strategies for implementing the policy.

Considering that health systems research is essentially concerned with the ways people seek and receive health services, the research can be focussed on the demand or the supply side of the health care equation. The demand side studies the needs, knowledge, attitudes and behaviour of individuals, households and populations with respect to their health. In contrast, the supply side studies are aimed at the providers of the services and the professional, intellectual, organizational, legal and political framework within which they work. I have stated earlier that the question of what determines how research findings become incorporated into health care actions is one area long due for health systems research study in Nigeria. There are several

others and I will just mention two which crop up frequently in discussions on health care in this country.

First, with the near total collapse of the public sector of the formal health care system in the country now, several alternative systems have sprung up — traditional herbal system, spiritual system, exorcism, divination and so on — and are flourishing. In this situation, people have had to assume almost total responsibility for their health and decide which of the parallel systems to select without the benefit of any authoritative information on the relative merits of the systems. Studies are needed to evaluate the relative strengths and weaknesses of the competing systems; what considerations determine the choices that people make, and how this relatively recent development has affected the health of the people and the economic growth of the country.

The second issue is health care in recent years. Most health care facilities have been informed by the need to satisfy the stringent conditionalities set by the International Monetary Fund (IMF) for bailing us out of our economic quagmire! But have these conditionalities helped or spelt disaster for the people's health? An example of this is the introduction of user fees in all our public sector health facilities for children and public servants who have hitherto enjoyed free health care. How has this change affected the use of the health care facilities by these groups and what has been its effect on their health and on national economic performance? Similarly, how have changes in drug policy, like the introduction of the Essential Drugs Programme, the Bamako Initiative and the Revolving Drug Fund with total cost recovery affected drug use and effective drug treatment of disease?

Clearly, these reforms have led to an increase in the cost of health care for the people. Health systems research would provide information on the extent of the increase and the impact of the increase on living standards, and on whether people are able or willing to absorb the increase. A health care system cannot be considered cost effective if it is so costly that the people for whom it is meant that they cannot patronize it, as we find in our major health care delivery facilities today.

Epilogue

It is my hope that enough data has been presented in this short address to emphasise the point that research is the foundation for effective health care. Health care providers need to recognise this fact and ensure that their policies and actions are firmly based on facts that have been derived from high quality research. In the same way, researchers should ensure that their studies are relevant to the health care problems of the country and are scientifically sound enough to provide the right answers to the existing problems. It is only in this way that the people would benefit from the resources — human and material — expended on health research.

In conclusion, I am mindful of the fact that the circumstances are not right in this country now for any kind of purposeful high quality research. The infrastructure for research which used to be quite adequate for our purposes are now outdated and completely run down, and there is no prospect — considering the level of health research funding — that they will soon be updated. Although qualified researchers are available and willing, there is little to motivate them to put in the type of effort

and personal sacrifice that resulted in the kind of research for which Osuntokun and his contemporaries were justifiably acclaimed. Nevertheless, we should not give up. Indeed, we cannot afford to give up.

I do not think anyone will dispute the fact that the two attributes of quality and relevance are the hallmarks of Osuntokun's research studies, and that he left us a legacy of hard work, dedication and commitment. His life was full of lessons for all of us, not least those of us who are interested in the promotion of health and the alleviation of disease through research. He strove for excellence in whatever he did, and was quick to recognise and admire excellence in others. The least we can do to ensure that he did not toil in vain is for all of us, in our own way, to continue to use our talents to the best of our ability, in the pursuit of the goal of better health for all our people.

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Benjamin Oluwakayode Osuntokun

MD PhD FMCP FWACP DSc OFR NNMA Hon DSc

Professor B.O. Osuntokun's works constitute a significant landmark in the history of the Medical School, University of Ibadan. It eloquently illustrates the heights attainable through sustained diligence and a robust, vibrant intellect in a literally science-unfriendly environment. Kayode did not see a Bunsen burner before entering the University of Ibadan, but rose to become one of Africa's most outstanding medical scientists, a scholar uniquely endowed with the gifts of profound erudition, intense dedication and prodigious energy. He touched nothing that he did not adorn.

A star performance in his undergraduate finals at Ibadan, in 1961, launched him into a remarkable career in medicine. Tutelage under some of Britain's leading clinical scientists of the day (Professor Harold Scarborough in Cardiff and Professor Henry Miller in Newcastle) ensured a sound template in Neurology and effortless ease with the British Membership of the College of Physicians. Windows of opportunity began to open one after another as Kayode's talents blossomed.

Returning to Ibadan in the mid-60s he set out to put African neurology on the global map, first by describing the natural

history of a number of neurological disorders in Africa. He then went on painstakingly to address, through a series of elegant clinical and biochemical studies, the simmering conflict in our understanding of the aetiopathogenesis of an intriguing form of ataxic neuropathy peculiar to sub-Saharan Africa linking it with toxicity of cyanogenetic glycosides in cassava. He took the neuropathies: epilepsy, cerebrovascular disorders, migraine and diabetes mellitus one by one, producing for each a classic treatise, with a tropical flavour, in some of the world's leading clinical and neurological journals. In subsequent years he turned his energies to Community Neurology and the Dementias of the Elderly. Whether at conference presentations, guest lectures, in chapters in books or as part of the over 300 publications in learned scientific journals, Kayode spoke or wrote with unusual depth and clarity, making original observations and indicating nuances of departure from established teaching.

In his global travels he can best be described as the *Marco Polo of African Neurology*, for there was hardly a world capital he did not visit to lecture. Such intense scientific activity inevitably resulted in a glittering array of prizes and distinctions, of which we can only name a few - The Sir Langley Memorial Prize for the best paper in Tropical Medicine (1968-71), The Murgatroyed Prize of the Royal College of Physicians of London for important contributions to Science, the Practice of Medicine in the Tropics (1977) and The Dr. Charles R. Drew World Medical Prize Award in 1989.

To these remarkable attributes we must add his foray into the wider turf of medical administration, medical education and health services research. Administration presented to him the exciting challenges of the Provostship of the famous Aro Neuropsychiatric Hospital and Chief Medical Director of Nigeria's premier teaching hospital — The University College Hospital at Ibadan. Medical Education earned him the Deanship of the Ibadan Medical School (1974-78), a tenure notable for a rapid expansion of undergraduate intake, physical consolidation and curricular development. Health Services research provided for him a pivotal position in the WHO Global Advisory Committee on Health Research (GACHR), that body's most prestigious health research policy organ.

Osuntokun's contributions as a clinical scientist to the work of the WHO will be difficult to surpass. With 120 Consultations as Temporary Adviser, Short-Term Consultant, and as Member of Expert Committees in a wide variety of subjects — at Headquarters in Geneva (sixty visits in 20 years) and at all of the Regional Offices — he straddled the vast expanse of WHO's activities like a colossus, eventually becoming the longest serving Member and Chairman of the GACHR. His term as Chairman of the global committee was notable for positive development following in the tradition of his predecessors, some of whom are Nobel Laureates. His interventions were invariably mature and sensible, always demonstrating a sound grasp of the subject and a human and humane perspective in proffering suggestions and solutions.

Back home in Nigeria, Professor Osuntokun's outstanding achievements were well acknowledged in the award of **Officer of the Federal Republic** (OFR) of Nigeria in 1978, and the **Nigerian National Merit Award** (NNMA) in 1984. It was largely through his academic and professional stature that Ibadan came to be designated by the Nigerian government as a Centre of Excellence in Neurosciences. Indeed, the Dementia project which death found in his hands represents an excellent example of a cross-cultural collaborative effort between Ibadan and Indiana University, and has attracted substantial funds from the National Institutes of Health in Bethesda, U.S., immense international prestige and considerable epidemiological experience to Ibadan. This project has come up with a number of fundamental observations in a virgin but critical area of research into the ageing process in a developing world milieu.

He is survived by his wife Olabopo, herself an accomplished Professor of Ophthalmology at the University of Ibadan, and five children, two of whom are medical doctors.