

**SOME HAVE
EYES
BUT CANNOT SEE**

BY

PROFESSOR AJESOLA A. MAJEKODUNMI



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SOME HAVE EYES BUT CANNOT SEE

An Inaugural Lecture Delivered at University of Lagos
Main Auditorium on Wednesday, August 17, 2005

by

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INTRODUCTION

Mr. Vice-Chancellor Sir, Prof. Oye Ibidapo-Obe, the Deputy Vice-Chancellor (Academic and Research) Prof. Soga Sofola, the Deputy Vice-Chancellor (Management Services) Prof. (Ven.) F.A. Fajemirokun, the Provost, College of Medicine University of Lagos (CMUL), Prof Steve Elesha, the Registrar, Mrs. Folashade Olumide, other Principal Officers of the University, Senate Members of The University, My Lords Spiritual and Temporal, My Past Teachers hereby present, Colleagues, Staff and Students from the CMUL and the Main Campus, Ophthalmologists in Public and Private sectors, Gentlemen of the Press, distinguished Ladies and Gentlemen. I thank the Vice-Chancellor for granting my request to deliver my Inaugural Lecture today, August 17th 2005. In few days time, August 21st 2005 to be precise, my youngest child, Olajide will be 30years old, and in addition, last month completed 30years of my continuous service to the University of Lagos. When I registered as the first female undergraduate of the University in 1962, and as one of the guinea-pigs of the University, little did I know that I was embarking on a long journey and career that will keep me within the walls of the university for my entire working life. Firstly, as a medical student, and later as a medical lecturer, I gradually and patiently climbed the academic ladder until I reached the pinnacle. This Inaugural lecture was therefore fixed to mark these important landmarks in my life.

As a medical student and young lecturer, one of the cultures of the academia that I admired and perhaps looked forward to was the ceremony of "Occupying the Chair" when a Professor was appointed. The ceremony usually followed the Inaugural lecture and specially conducted by the Provost of the College. The "Chair" bore the name and the specialty of the Professor and the latter was expected to sit on his/her "throne" whenever he/she was in the office. Being a personal chair, it was one of the belongings that the Professor took away on retirement. This short ceremony was an inspiration to the junior ones and something to look forward to.

Mr. Vice-Chancellor, Sir, I hope you will revive this old culture during your tenure.

Inaugural lecture is a debt that every Professor must pay to mark his/her arrival at the final destination of one's academic career. Mine is thus an overdue debt and I thank God for sparing my life to pay the debt I owe.

Mr. Vice-Chancellor Sir, during this lecture, I intend to take my audience through a panoramic view of the Eye – this very important but small organ, then talk about No eyes, No sight, discuss some causes of blindness and what we have been able to do to help such people in my practice over the years.

There are 5 Special Senses:

- Sense of SIGHT;
- Sense of HEARING;
- Sense of SMELL;
- Sense of TASTE; and
- Sense of TOUCH.

The most developed and the most important of these Senses is the sense of SIGHT.

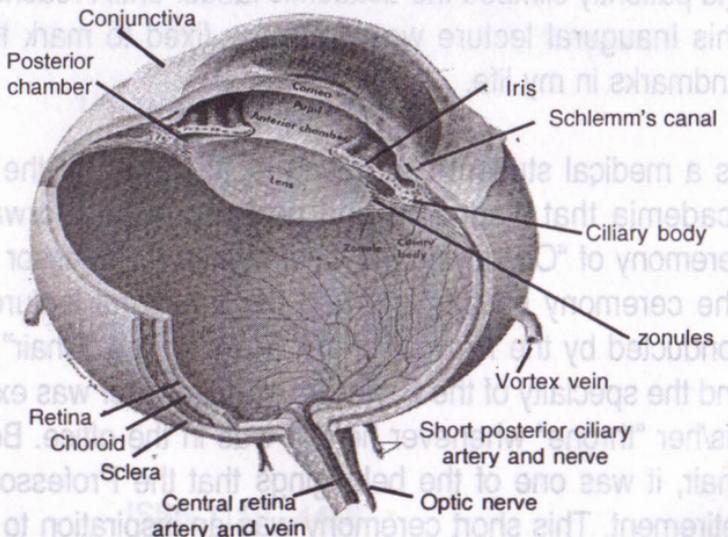


Fig. 1: The Human Eye

In a nutshell, the eyeball has 3 coats – outer protective coat, made up of the Sclera, and the transparent Cornea both continuous at the corneoscleral junction – the Limbus; the middle, nutrient coat of the eye, the Uvea (the Iris, Ciliary body and the Choroid) and the innermost neural coat of the eye – the Retina. The retina contains about 120 million Rods and 5million Cones, the Photoreceptors. Its nerve fibres leave the eyeball via the Optic nerve. The optic nerve, the 2nd cranial nerve contains over 1million fibres. So the distribution of the photoreceptors to the optic nerve fibres cannot be uniform. At the fovea, the most central and sensitive part of the retina, there is a high concentration of cones and their connection to the fibres are more specific, whereas at the periphery of the retina, where the rods are concentrated, their connections to the optic nerve fibres are less specific.

Intraocularly behind the iris lies the crystalline Lens, suspended in the eye by the Suspensory Ligaments attached to the ciliary muscles.

The Anterior and Posterior chambers are the Aqueous chambers containing Aqueous Humour (AH), the nutrient fluid of the eye. Behind the lens is the Vitreous chamber containing the jelly-like Vitreous Humour.

The Cornea is responsible for 70-80% of the eye's refractive power whilst the Lens accounts for 20-30%. We can therefore refer to the two as the light-focusing tissues of the eye.

Currently, "Spare Parts" in form of donated cornea and intraocular lenses are available for the replacement of these two important avascular tissues when diseased.

The Limbus contains the Trabecular Meshwork (TM) that I shall talk about more, later in the lecture. It also provides an ideal point of entry into the eye during surgery. Fig. 2

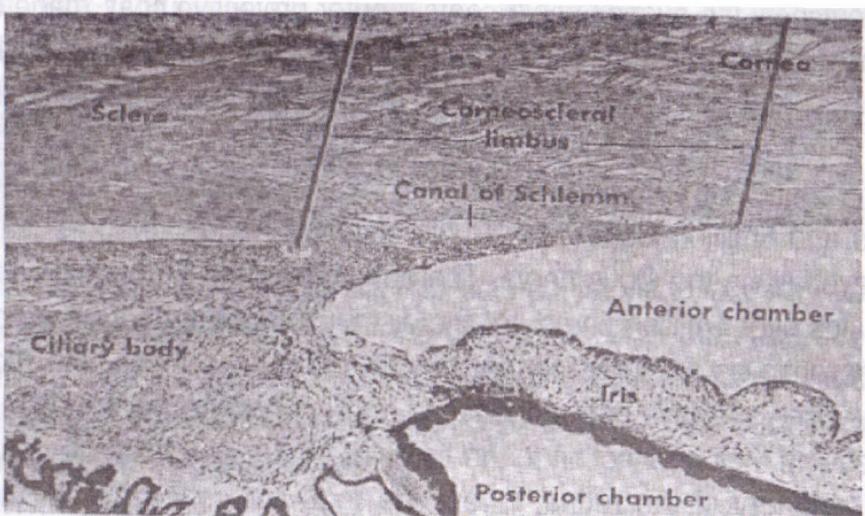


Fig. 2: Drainage Angle of the Eye and Canal of Schlemm

The aqueous humour (AH) is produced by the non-pigmented epithelium of the ciliary body. It is not only the nutrient fluid of the eye but also maintains the intraocular pressure (IOP). In a cycle, the AH when produced, is discharged into the posterior chamber and passes through the pupil into the anterior chamber (AC). It leaves the AC, passes through the drainage angle, through the TM into the Canal of Schlemm (CS). It is collected from the CS by the collector channels to the intrascleral plexus of veins and subsequently, into the episcleral veins.

The intraocular pressure (IOP) at any given time is therefore the balance between constant AH production and consistent outflow. Fig. 3



AP

AF



AP +

AF -

Fig. 3:

Theoretically, a disturbance of this equilibrium either due to increase AH production or decrease in its outflow will result in elevated IOP.

MECHANISM OF VISION

The cones are responsible for day vision (photopic vision) while the rods are mainly for night vision (scotopic vision). When the light enters the eye, it is focused on the fovea by the cornea and the lens. The light stimulus is converted into electro-chemical impulses by the receptors depending on the time of the day. The impulses are then transmitted along the visual pathway into the cerebral cortex where they are interpreted and presented as images or pictures of the objects seen. Therefore, under normal conditions, everybody who has eyes, intact visual pathway and cortex should see.

ANOMALIES OF VISION

But is it every human that have eyes? Congenital abnormalities may arise as an arrest of development of the foetus from the fertilized egg. This also applies to the eye. During the development of the foetus especially in the 1st trimester of pregnancy, the eye rudiments may be "lost" due to chromosomal abnormalities (Patau's Syndrome; D trisomy), infection (Rubella syndrome), drug ingestion or idiopathic. On the other hand, the eyes may be absent at birth (anophthalmos). We reported few cases of anophthalmos seen at LUTH in 1977¹. Fig. 4 & Fig. 5.



Fig. 4: Anophthalmos



Fig. 5: Anophthalmos. Examination Under Anaesthesia

So some do not have eyes and understandably cannot see. They have never seen before and so grow into adulthood losing nothing. But majority are born with eyes and can see. The natural pattern is that many should have eyes to see, or else we will be living in the "World or Countries of the Blind".

BUT SOME HAVE EYES BUT CANNOT SEE. This Lecture will revolve around the causes, what we have done for such patients over the years, and how these causes can be minimized or eradicated.

CAUSES OF BLINDNESS IN AFRICA

Blindness according to WHO is defined as visual acuity less than 3/60 in the better eye with best correction or central visual field less than 10° from the centre of fixation. Blindness is a major health, social and economic problem especially in the developing countries. The enormity of the problem becomes significant when we consider that there are about 45million blind people in the world and approximately 7.1% (3.2million) of them live in Sub-Saharan Africa². This blinding problem is associated with backwardness, poverty, poor hygiene, lack of preventive and curative health services, prevalence of superstitious

and unhealthy beliefs and customs, coupled with ignorance and low level of health awareness. Half of the blindness is due to cataract and about 15% due to glaucoma.³ More than half of these blind people, indeed about 60% are women with an age adjusted risk of blindness 1.39times that of men.^{4,5}

BLINDNESS IN NIGERIA

The blindness rate in Nigeria is 1.3%. With a population of 120million, this translates to the fact that 1.6million Nigerians are blind. Most of the blindness surveys in the country are community, States, or Local Government based.⁶⁻⁸

A national survey of blindness and low vision is currently going on. The causes of blindness are Cataract, Glaucoma, Corneal Diseases, Onchocerciasis and Trachoma . Half of the blindness is due to cataract.^{7,8} Glaucoma is the second cause of blindness in Nigeria.

CATARACT

Cataract is opacity of the crystalline lens and the most common cause is senility.



Fig. 6: Patient with Matured Senile Cataract

About half of the global blindness, including Nigeria is due to cataract.³ The public health importance of cataract is the reversibility of its blindness. That is, it is a treatable cause of blindness. Cataract presents with painless, gradual loss of vision. Like most diseases in the blacks, it tends to present at an earlier age compared to the Caucasians.^{22,1}

Some years back, we looked at some of the possible explanation for this in relation to the components of the cataract in the blacks. Alao and Majekodunmi⁹ studied the physical characteristics of the Human Senile Cataract and found that the brown dense cataract is more common in Nigerian cataractous lenses and that the colour of the cataract varies from yellow to brown depending on the age of the patient. We deduced that this change in colour might be due to the effect of the ultra-violet (UV) light exposure in the tropics, comparing this to the relationship between UV light and pterygium.

We also studied the biochemical composition of the senile cataract in Nigerians with relations to Vit. C. We reported that in the dark-brown cataract, the level of Ascorbic Acid (Vit. C) is very low (almost nil) compared to the findings in Caucasians, and that the darker the lens, the less the Vit. C content. Since the dark-brown cataracts were in the very old patients, we concluded that the older the patient, the lower the Vit. C content in the cataract.¹⁰ We could not relate these findings to the Vit. C intake of the patients.

The Only Treatment for Cataract is Surgery

In the past (although this type of surgery is still performed in some centres in Nigeria) we performed the intracapsular cataract extraction, a procedure whereby the lens is removed in toto from the eye. An aphakic lens (thick bulky lens) is given to the patient post operatively (Fig 7).



Fig. 7: Patient with Aphakic Lens Spectacle

The operation was easier to perform, cheaper, technologically simpler and gives good visual outcome. But it is cosmetically unacceptable and optically associated with lots of complaints such as image enlargement and reduced peripheral fields. This is due to the fact that the substituted lens is not in its natural position, which is within the eye. In this era of modern appropriate technology and microsurgical technique, we now perform the extra-capsular cataract extraction. In this procedure, the anterior capsule and nucleus of lens are removed, and an intraocular lens (IOL) is placed on the posterior capsule in the posterior chamber, the natural position of the lens. The IOLS used are shown in Figs. 8 & 9.

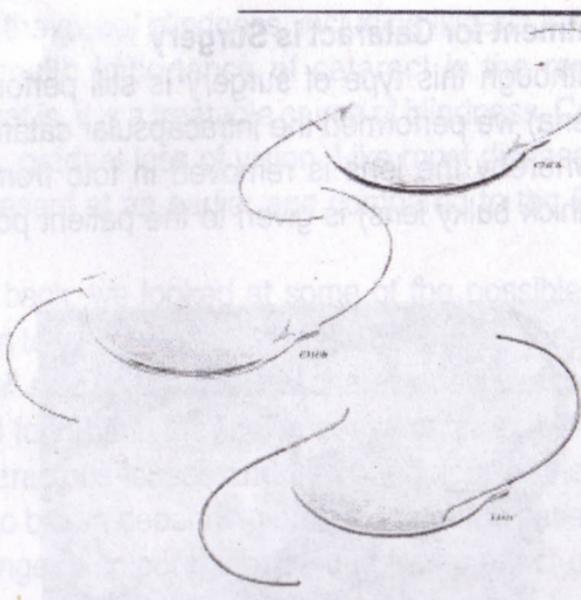


Fig. 8: Intraocular Lenses

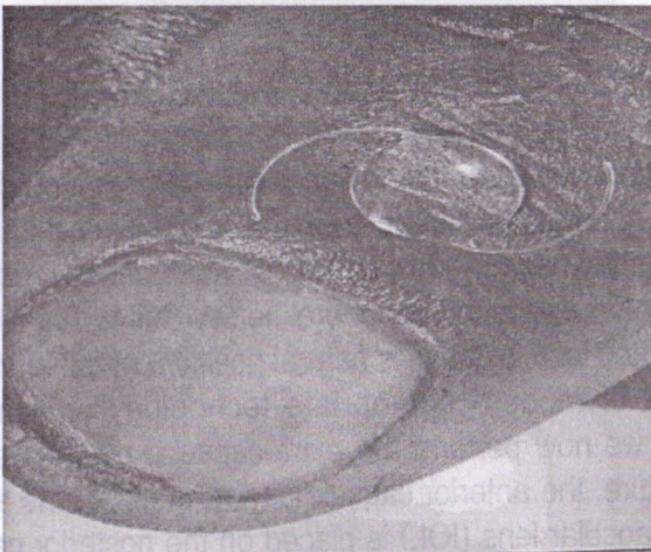


Fig. 9: Intraocular Lens Size Relative to the Thumb (Courtesy of Fred Hollows)

With this technique, though expensive, patients with cataractous lens can see right from the operating table after the insertion of the IOL. The success rate is 95%. So, we can claim that like the biblical saying *"We make the blind to see"*.

CORNEAL DISEASES

Blindness from corneal scars due to Vitamin A deficiency, trachoma, onchocerciasis, measles and trauma is preventable. This can be achieved by diet rich in Vitamin A or distribution of Vitamin A capsules to children and needy adults to supplement their diet. Some years ago, distribution of Vitamin A to children during immunization against polio and measles was introduced in Nigeria as a preventive measure against blindness from Vitamin A deficiency. Currently, with the assistance of UNICEF and NAFDAC, Vit. A is now added to flour, salt and vegetable cooking oil. Immunization of children against measles has also reduced corneal scars due to measles keratitis.

Blindness from corneal scars can be treated by surgery. Corneal graft, (corneal transplant or keratoplasty) is readily available but the difficulty is in obtaining the donor eyes! The Decree No 23 of 1973 permits cornea to be removed after death from human donors. It is however sad that donation of eyes after death is still not popular in our environment due to ignorance and unhealthy social customs. Currently the donor corneae used in Nigeria are from abroad and surely not of the best grade.

The first Eye Bank in the country is just being established in Lagos. I believe that the result of corneal transplant will improve with the use of fresh specimens from our Bank. In a big country like Nigeria, more Eye Banks are needed. Voluntary organizations, governments and Private entrepreneurs can establish Eye Banks. I appeal to you all to donate your eyes after death so that some who have Eyes Can See again.

ONCHOCERCIASIS

Onchocerciasis, also known as River blindness because the fly, *Simulium damnosum* that transmits the microfilaria from man to man stays around fresh, fast flowing rivers. A small worm, *onchocerca volvulus*, causes it. See figure 10.

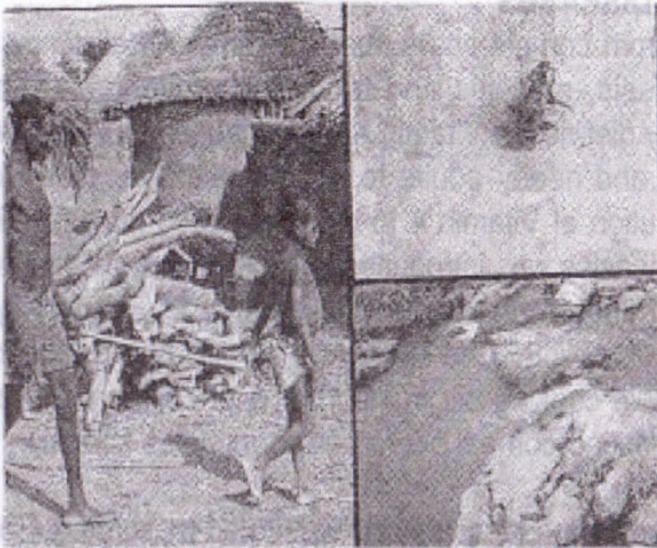


Fig. 10: Onchocerciasis: (left) a blind man being led by a boy, (upper right) Simulium fly (lower right) fresh water river, (courtesy WHO teaching slides)

Onchocerciasis occurs in about 30 African countries from Senegal in the West through Ethiopia in the East and down to Malawi in the South. Reports show that about 18million people are infested by *Onchocerca volvulus*, the adult worm and some 270,000 people are blind from the disease¹¹. Surprisingly, the blinding onchocerciasis is mainly in West Africa. It is still endemic in some parts of the North of the country.

With the introduction of Ivermectin tablets by Merck & Co. in the 80s, blindness from Onchocerciasis has reduced tremendously. For effective treatment, however Ivermectin tablets need to be taken annually for 10-15years. Although, eradication of Onchocerciasis may not be readily feasible, its blindness may be controlled or reduced to the minimum. One of the strategic measures being taken towards this is the Community Directed Treatment with Ivermectin (CDTI). In our environment this is not without its own problems. Some of the problems encountered in the distribution of the tablets are poor infrastructure e.g. bad roads, poor drug compliance and inavailability of alternate potable water supply.

TRACHOMA

One of the earliest reported causes of blindness is trachoma (Egyptian Ophthalmia). It was described in the early BC and its effective treatment with copper sulphate by Egyptians was widely advocated. It is believed that the soldiers who returned from Egypt after the 1st and 2nd World Wars introduced trachoma into Nigeria. Surprisingly, Trachoma is still a common cause of preventable blindness worldwide, and also in the Northern part of Nigeria. It is a disease of low socio-economic class, and more common in women and children. While doing some studies on trichiasis at the ECWA Eye Hospital Kano in 1982, I noticed that trachoma was quite common in women in "Purdah". Interviewing these women revealed that the senior wife shared her antimony applicator with her junior mates and the young children of the family! The adage "prevention is better and cheaper than cure" is best applied to trachoma. A report from Saudi Arabia¹² showed that less than US\$1 per patient is all that is required to prevent trachoma, but thousands of dollars may be needed to cure its complications such as trichiasis and corneal scar. Personal hygiene, provision of potable water to wash the face thrice daily, wearing of facial condom, control of house flies from transmitting the disease by appropriate waste disposal method, improved housing conditions and public enlightenment are known measures that can be taken to prevent or reduce the disease.^{13,14}

Trachoma in the active stage is treated with Terramycin. The patient is placed on this eye ointment four times daily for about a year. For better compliance, an alternative mode of treatment needs to be sought. Introduction of a single oral dose of Azithromycin 20mg/kg has shown that this is as effective as topical terramycin in the treatment of the disease^{11,12}. Trachoma infection and blindness were reduced by 50%¹² after preventive and therapeutic measures were taken over a decade.

Trichiasis, the major cause of corneal scar and blindness in this disease is treated by surgery or cryotherapy. In 1981, we tried our hands on the effectivity of cryosurgery in the treatment of Trichiasis. This was after a

trip to ECWA Eye hospital, Kano, the 1st eye hospital in Nigeria, where I saw many cases of trichomatous trichiasis with impending blindness. Using rabbits, we tried the effect of frozen carbon dioxide gas (-4°C) applied to the follicles of the eyelashes, using freeze and thaw technique. Here I must acknowledge the assistance of Prof. Oyin Elebute, Professor of Physiology, who came to my rescue after I have lost few rabbits in a day! She became my laboratory supervisor throughout the project.

Having perfected my technique on rabbits, at the Animal House CMUL, I proceeded to treat patients with trichiasis at ECWA eye hospital Kano. The treatment was effective and the result was published in *British Journal of Ophthalmology*.¹⁷

Currently, the disease strategy for trachoma is the SAFE strategy (Surgery or Cryosurgery for trichiasis, Antibiotics for active infection, Facial cleanliness for reduction in transmission and Environmental improvement to remove risk factors).

A vaccine that will be effective against trachoma is still to be developed. So far, the vaccine produced provides a short immunity, and sensitizes the patient who develops a more severe ocular disease than the control. I believe that with all the measures being taken to combat the disease currently in Nigeria, trachoma like smallpox infection will soon be a disease of the past. Then those who have eyes can see.

GLAUCOMA

Although this is the second common cause of blindness, I have deliberately decided to treat this topic last as it is the most common cause of SOME HAVE EYES BUT CAN NOT SEE (NWON LA OJU SILE SUGBON NWON KO RIRAN; UFONDI NWERE ANYA MA HA D'GHI AFU UZO; WA DENSU SU NA DE IDO A MA BA SU A GANI).

Over 3million people worldwide are glaucoma blind. The most common type of glaucoma is the Primary Open Angle Glaucoma.^{18,19} Also known as silent Blinder, or the Thief of the Night, it is 3-4x more common in the blacks than the Caucasians and develops at an earlier age in the blacks.

What is Primary Open Angle Glaucoma?

This is a blinding disease, multifactorial, and of insidious onset characterized by optic nerve head damage, visual field loss with open drainage angle of the eye. Some of the risk factors are elevated intraocular pressure, heredity, myopia, race, colour, diabetes and hypertension. The most investigated of these factors is the IOP, and treatments so far have been directed to lowering the IOP.

My interest in this disease began in 1972 when I had the opportunity of working at the Courage Laboratory, Royal Eye Hospital, London under Mr. Alan Friedmann, the designer of Friedmann Visual Field Analyser. Alan's life revolved round POAG, which according to him, "is a disease of unknown aetiology, leading to blindness despite medical therapy" Most of the patient we saw who were blind with POAG were blacks and relatively younger than the whites. Alan threw a challenge at me after one of the clinical sessions when he said, "You have to look more into this disease being black yourself and I bet you have a problem back home". Indeed, I had, or I have, as Alan's statement 30years ago is still back.



The Glaucoma train took me to Bristol in the 80s where I met Mr. Vincent J. Marmion of Bristol Eye Hospital, a glaucomatologist, my friend, adviser and mentor. A man of many parts, Vincent is a committed catholic, an excellent clinician, a sound researcher, a patient teacher, a strict examiner, but above all, a devoted family man. At 76, Vincent still sends me e-mails regularly on topics related to POAG.

PRIMARY OPEN ANGLE GLAUCOMA IN NIGERIA

That POAG is an important cause of blindness in Nigeria cannot be over-emphasised. It accounts for 60% of all glaucomas seen in our clinic.¹⁸ In our study of the pattern of eye diseases in adults 16years and above in Ikeja and Alimoso Local Government Areas of Lagos state in 1995, POAG was the second cause of blindness.²⁰

That POAG is hereditary has been established in our Glaucoma clinic where we have on records 3 generations of patients in addition to siblings and other blood relations. Management of POAG patients is associated with problems some of which are peculiar to us. These are late presentation, ignorance, illiteracy and poverty. Many of the patients live in the rural areas far from the urban areas where the treatment is available. There are only 300 Ophthalmologists in the country and most of them are based in the cities.

In the 70s, the medical treatment was with Pilocarpine eye drops (miotics) and Acetazolamide tablets. With the introduction of β -blockers e.g. Timolol maleate in 1974, drug compliance improved tremendously. But these drugs are more expensive than pilocarpine, and have undesirable side effects such as bradycardia.

The last decade has seen the emergence of prostaglandin analogues e.g. Latanoprost etc. These are very potent drugs applied only once a day, but cost-wise are beyond the reach of the common patient. In developed countries, such drugs are supplied to patients either free or at a heavily subsidized price. Unfortunately, unlike the treatment of

cataract, that of POAG is not “as marketable and cost effective”. In fact, the treatment in POAG is not to improve vision but to control or reduce the progression of the disease. Like diabetes mellitus, POAG cannot be cured. Therefore, many patients find it difficult to continue with their treatment when they cannot see an improvement in their vision.

Problems Associated with medical treatment of POAG as seen in Nigeria¹⁵ are listed in Table 1.

Table 1: Problems of Medical Treatment of POAG

Inavailability of drugs
Expensive drugs
Fake/Expired drugs
Poor attendance at follow up clinic
Poor patient drug compliance
Poly pharmacy

Over the years it became obvious that an alternative but definitive treatment has to be sorted for the treatment of POAG. *We now know that surgery is the best treatment for POAG.* In the past, various types of surgical procedures have evolved. These included trephination, iridenclysis, and Scheie’s operation. Indication for surgery then was persistently raised intraocular pressure (IOP) despite adequate medical therapy. Nowadays, medical treatment is initiated to lower the IOP in preparation for surgery. Currently, the treatment of choice for POAG is TRABECULECTOMY.^{22,23} The advantages of surgery are shown in Table 2.

Table 2: Advantages of Surgery

Cheaper treatment on the long run
Continuous drainage of aqueous
Fewer follow up clinic appointments
Eliminated or reduced fear of compliance
Convenience for patients

In 1968, Cairns developed a drainage operation whereby a fistula is created between the anterior chamber and the conjunctiva to allow the aqueous to drain continuously, thus supplementing the natural drainage. This operation has stood the test of time and modified by different surgeons accordingly. Our trabeculectomy procedure best in our hands is shown in the sketch below (Fig 8)

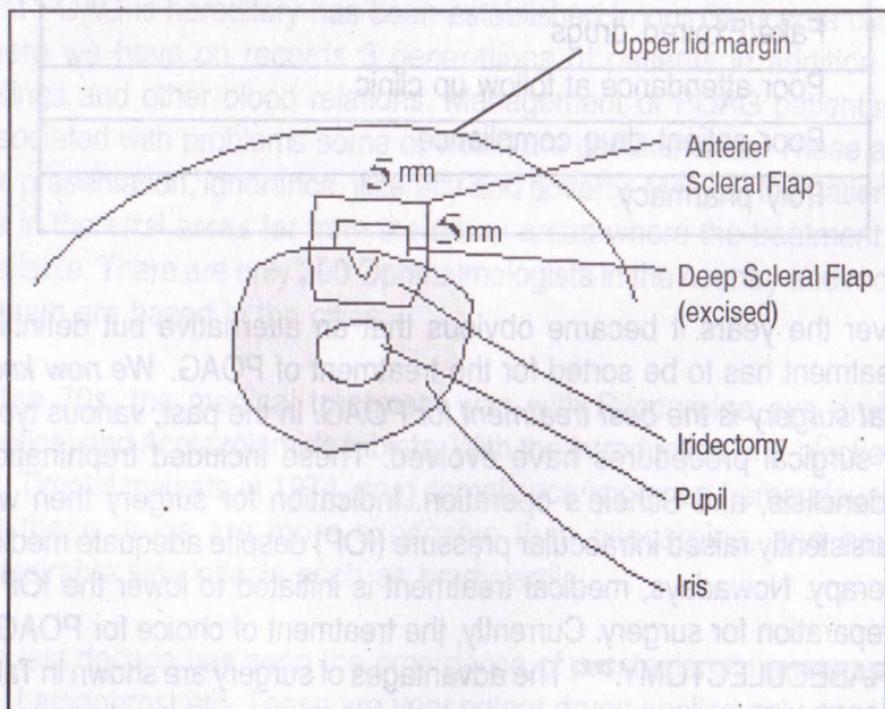
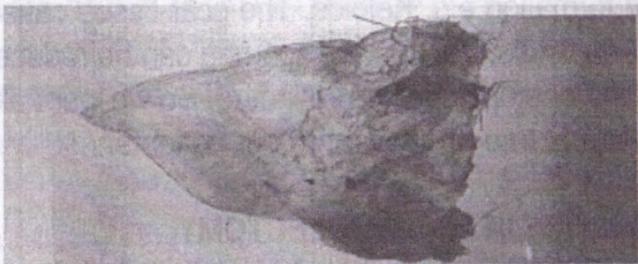


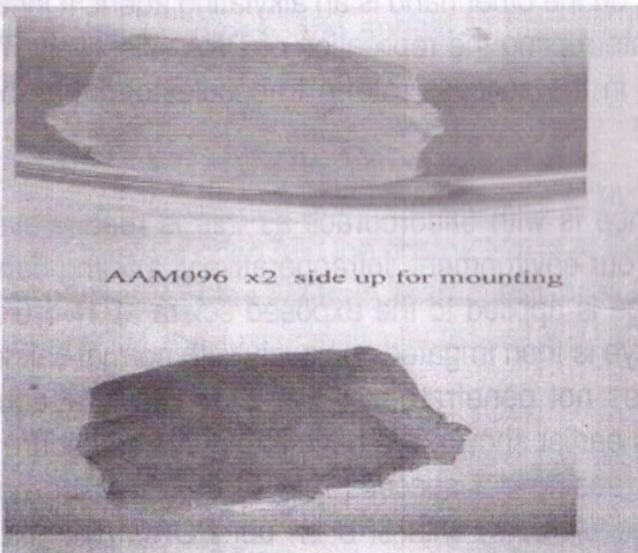
Fig. 8: Trabeculectomy procedure



AAM03. x2.



AAM07a. x2.



AAM096 x2 side up for mounting

Fig. 10: TM specimen x 80

Figs. 9 & 10 above show the specimens, of the TM excised x 80 of the actual size.

The success rate of this procedure in our hands is 65-70% compared to that of 70-80% in the white patients. This difference may be due to the tendency to scar formation in the blacks. We know that blacks are

prone to scar formation e.g. Keloids. The scar tissue causes stenosis or closure of the fistula. Therefore if scarring can be reduced, stenosis or closure of the opening can be prevented. So we went ahead to see if this hypothesis is true or relevant to our patients.

ANTIMETABOLITES IN TRABECULECTOMY

Antimetabolites are known for their inhibition of cellular proliferation, hence their usefulness in malignancy. Post trabeculectomy fibroblastic activities can be suppressed by the use of antimetabolites. We put this to test in our patients.

The two commonly used antimetabolites in ophthalmic practice are 5Fluorouracil (5FU) and Mitomycin C (MMC). 5FU is pyrimidine analogue, which blocks DNA production by the inhibition of thymidylate synthesis. Mitomycin C, on the other hand is an alkylating agent. It inhibits cellular mitosis, by interrupting the replication of DNA selectively. Their role in the increase in the success rate in trabeculectomy has been widely reported. ²⁴⁻²⁷

Our experience is with 5fluorouracil as this is readily available and affordable in our environment. Intraoperatively, a 50mg dab of 5FU on a microsponge is applied to the exposed sclera at 11-1 0'clock for 3-5mins. The eye is then irrigated copiously with normal saline to ensure that 5FU does not penetrate into the eye. Then trabeculectomy is performed as earlier shown. We have found this procedure useful and effective, increasing our success rate to 80-90%. We now perform routinely trabeculectomy with 5FU on our POAG patients. In clinical terms, patients with filtering blebs (fistula) have continuous AH drainage, low IOP and controlled disease. In addition they do not need to apply antiglaucoma drugs, thus saving cost. In few that may require additional drops later, poly pharmacy is never the case.

PROBLEMS ASSOCIATED WITH SURGICAL TREATMENT OF POAG

Table 3 shows some of the problems associated with the surgical treatment of POAG peculiar to our environment as encountered.²⁸

Table 3: Problems of Surgical Treatment in POAG

Dearth of manpower
Cost of surgery
Failure of surgery but repeatable
Fear of Anaesthesia
Fear of hospital routine/poor acceptance of surgery
Extra hand required postoperatively and its economic effect

We have tried to break these barriers through public enlightenment, giving talks to patients on their first visit to hospital, local production of some affordable eyedrops, and appeal to hospital management for reduction in surgical fees.

CURRENT RESEARCH ON POAG

Current research is directed at the aetiology of POAG. We know that the drainage angle is open and the obstruction is at the level of the TM. The functional parts of the TM from internal outwards are the uveal TM, corneo-scleral TM, the Juxtacanalicular tissue (JCT) and the Endothelial or single layer inner wall (Fig. 11).

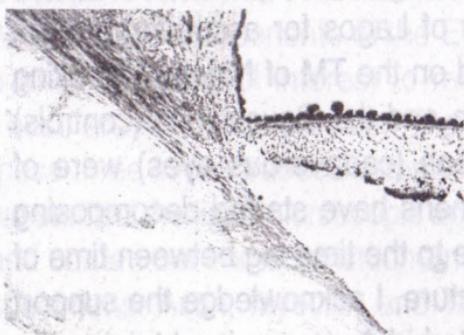


Fig. 11: TM x 300



Fig. 11: TM x 880

It is the JCT that contributes a major obstruction to the aqueous outflow in POAG, partly due to its narrow pathway and the macromolecular elements in the extracellular matrix (ECM). The role of the ECM and the extent of its genetic involvement in POAG are being investigated at the molecular level.

During my Sabbatical leave spent at the Experimental Ophthalmology Unit (EOU) of the University of Liverpool, I had the opportunity of working in the Laboratory of Prof. Ian Grierson, one of the leading authorities in Europe on TM in POAG.



Glaucoma Team: Experimental Ophthalmology Unit,
The University of Liverpool Oct. 2003 - Aug. 2004

It was a beneficial year (October 2003-August 2004) that I shall never forget. I am grateful to the University of Lagos for according me the opportunity. While in EOU, we worked on the TM of Nigerians looking at the differences between the African and the Caucasians (controls) TM. The African TM control specimens (cadaverous eyes) were of poor qualities and most of the specimens have started decomposing before fixing in Formalin. This was due to the time lag between time of death and trabeculectomy. At this juncture, I acknowledge the support of Prof Steve Elesha, Professor of Morbid Anatomy, in obtaining the control specimens.

In the normal eyes, the TM secretes ECM components and enzymes necessary for its survival (e.g. myocillin²⁹⁻³¹, thrombospondins³²⁻³⁴ and Actin³⁵⁻³⁷). Other functions of TM include phagocytosis, contractility, cell proliferation and response to stress.

Like other tissues in the body, the TM undergoes age-related changes. It is relevant and important that the age-related changes of the TM are highlighted so as to provide a baseline for comparison with POAG specimens.

We know that POAG is predominant in older age groups¹⁸ and in some population over 5% of people over 65 years have POAG¹⁹.

The changes in TM as seen in POAG are similar to those seen in ageing eyes but in a more severe form.³⁸ These include cell loss, significantly lower cell nucleus number and increase in ECM. The number of cells containing melanin in the cytoplasm of the TM cells increases in POAG, but there is reduction of the intercellular trabecular spaces. The causes of these marked changes in POAG and not in the age-matched controls are some of the questions to be addressed in future studies. *What are the cytological changes in the TM of black POAG patients due to? Are these due to environmental or racial factors?* We did not find any increase in the melanin pigment of our TM specimens.

CURRENT AND FUTURE RESEARCH INTERESTS

Amongst the components of the ECM currently in focus, I will highlight 3 of which were of interest to me while I was on Sabbatical leave. These are Actin, Myocilin and Thrombospondin 1&2. With reference to these three in the trabeculectomy specimens of Nigerians with POAG, we studied the light microscopic appearance in some of our specimens, and carried out immunohistochemical assays on both controls and our specimens. Actin, Myocilin and Thrombospondin were demonstrated immunochemically in our control. We are still analyzing the results in our specimens.

Actin

This is a cytoplasmic cytoskeletal filament and one of the major intracellular proteins thickly arranged either in bundles or isolated. It was first reported in vervet monkeys in the endothelial cells of the walls of SC³⁹. It has since been identified in human uveal, corneoscleral and JCT meshwork cells along the basal cytoplasm³⁷. There are two types of Actin – the large microfilaments and the fine microfilaments. Functionally, Actin maintains the structural integrity and normal functions of the TM⁴⁰; stabilises cells by associating with adhesion plaques, thus acting as cytoskeletal struts⁴¹; link cells, by maintaining contact amongst the cells; contracts, opening up the intercellular spaces, and phagocytose cell debris.

The relevance of Actin to POAG lies in the fact that with the presence of its filaments in TM, JCT and endothelium of the SC wall, it is possible that the contractile function of the Actin filaments have a role in the regulation of outflow facility of AH by enhancing e sy formation of giant vacuoles, or effecting a change in the architecture of the intertrabecular spaces of the TM. Reduction of the Actin filaments architecture and contractility may lead to increase resistance to aqueous outflow and affect the regulation of IOP.

Thrombospondins (TSP)

Thrombospondins are structural matricellular glycoprotein of extracellular matrix joined by disulfide bonds. Currently it consists of 5 members TSP 1,2,3,4, &5, but TSP 1&2 are more widely distributed⁴². It is found in the basement membrane of TM, its ECM and intracellular structure and in AH and vitreous⁴³. The functions of TSP are reduction of cell adhesion, destabilisation of cell adhesion, cell migration inducement⁴⁴ and promotion of angiogenesis⁴⁵ and probably plays a role in loss of cellularity in TM of ageing eye and POAG⁴⁶.

Because of the presence of TSP in ECM, and its role in maintenance of adhesions of TBM cells of its beams, TSP may be important in the

modulation of aqueous outflow in glaucomatous and normal eye. If TSP promotes angiogenesis and its secretion diminishes in presence of high glucose level, then TSP may be important in diabetics with glaucoma as it is known that angiogenesis is more common in diabetic patients, and there is believed to be a relationship between POAG and diabetes.

Myocilin (TIGR)

Myocilin is an intracellular and extracellular glycoprotein also known as Trabecular Meshwork Inducible Glucocorticoid Response (TIGR). Isolated in 1998^{47,48} this protein was named Myocilin with a gene symbol MYOC. It was the 1st gene to be mapped to Juvenile Open Angle Glaucoma and POAG. It is located to chromosome region 1q23-24. Recently it has been reported in different population.^{49,50}

It has been located in human TM^{47,48} ciliary body.⁵¹ Its nonpigmented epithelium⁵², iris⁵¹, cornea⁵³, sclera & optic nerve⁵² and aqueous humour.⁵³ That myocilin is present intracellularly around the nucleus was demonstrated and reported⁵⁴, and secreted from glucocorticoid treated human TM. Myocilin has several structured features for interaction with glycosaminoglycans (GAGs) and other glycoproteins⁵⁵ and is a major stress response protein in human TM. Its induction by glucocorticoids is decreased by fibroblast growth factor and TGF-beta. The function of myocilin still eludes our understanding and the mechanisms by which its gene leads to glaucoma is unknown. However we know that myocilin is a microtubular binding protein.⁵⁶

The importance of myocilin with respect to POAG is based on evidence that it plays vital role in the pathogenesis of POAG. It is expressed more in TM than in other tissues, increases with age and much more so in the TM of patients with POAG.⁵⁷ Through interaction with other ECM elements, it may be crucial in the maintenance of normal aqueous flow and increase in its expression may lead to increase aqueous flow resistance and increase IOP.⁵⁸

Also, recent studies show that myocilin is a hydrophobic protein, tightly bound to polycarbonate filters and may obstruct the flow through the small pores such as those seen in JCT. The impediment to aqueous flow may be an important factor in increase resistance of flow through the pathway.^{53, 59}

We intend to continue this important work in collaboration with the Experimental Ophthalmology Unit, the University of Liverpool and Our Unit. The study will be cheaper for us however if the University of Lagos can establish a Central Research Laboratory, where most of this research can be carried out.

CONCLUSION

I have gone through the reasons why some without eyes cannot see. We have dealt with causes of why some have eyes but cannot see in relation to blindness in Nigeria with emphasis on POAG. In so doing, POAG was defined, its severity in our environment and the difficulties encountered in our management of the disease, and how we tackled them were highlighted. The current and future research on this "Thief of the Night" as related to the blacks was mentioned.

The genetic angle and the role of ECM in POAG with relation to its aetiology seem to be the questions still to be answered through research. I believe that the aetiology of POAG, like sickle cell disease will be known before the middle of this Century. To achieve this, the clinical studies of this disease are not enough. Laboratory research must be encouraged in young academic ophthalmologists backed with adequate funding. We, the African Ophthalmologists must join hands to find solution to POAG, the second common cause of blindness in our society. This is the only way that we can ensure that **SOME WHO HAVE EYES CAN SEE.**

RECOMMENDATIONS

I recommend that:

- The Federal and State Governments, Non-Governmental Organizations and Private Sectors join hands in public enlightenment of POAG through electronic and print media and radio jingles.
- National Glaucoma Association is formed as in line with other health related associations.
- POAG patients be exempted from consultation fees at government hospitals as it is an incurable disease
- The cost of Antiglaucoma drugs be subsidized by government and made affordable to the patients or on the alternative, low-cost eye drops are produced by the pharmacy department of the specialist and tertiary hospitals.
- Staff of the University of Lagos 50 years and above should have free, eye screening organized by the University once a year.
- Trabeculectomy should be free or made affordable to the common man.
- The one-year abroad part of the residency training be reinstated and the period be spent equally between laboratory research and clinical work.
- Newly appointed Lecturer I at Colleges of Medicine be sent abroad for 1 year fellowship in research work related to their clinical specialty.
- Government and manufacturing companies should allocate more funds to research work.
- At least once in 7 years clinicians in academics should be encouraged to spend their Sabbatical year doing laboratory research work in their field.

ACKNOWLEDGEMENTS

I thank the Almighty God for His mercies in my academic journey over the past 30 years and so I raise my “Ebenezer” today.

My thanks and gratitude go to my parents late Mr. Alfred Awokoya and Mrs. Jemima Olabopo Solarin for giving me the opportunity of a sound education at the time when the education of the girl-child was frowned upon. Perhaps Dad had no choice as he had 3 daughters and wanted to show that what boys can do, girls can do better. He was always proud of his daughters. Mum (alias Madam) was a teacher and the Margaret Thatcher of the family. She believes in extended family and ensured that her brothers and cousins were all well educated. She would have been here today but the mobility of a 92 year old is limited.



Mr & Mrs Solarin on the occasion of their 50th Wedding Anniversary

I believe my parents were not let down by their daughters; Ajesola and Oluremi, (an anaesthetist and former Chief Consultant in charge of Ring Road Hospital, Ibadan) are medical doctors and late Adeola, was the Chief Medical Records Officer, Psychiatrist Hospital, Yaba. They brought us up in a disciplined, happy Christian home with the fear of God instilled in us.

To my teachers at Methodist Girls High School Yaba, I cannot but be grateful particularly to Mrs. Kehinde Abayomi (Nee Smith). She was my role model, and taught me not only Biology but also how to walk with shoulders raised. I am grateful. Mrs Deborah Oso (Nee Jaiyesimi) was Mathematics personified; she taught me Mathematics and almost succeeded in making me a Mathematics teacher.

After my secondary education, I was encouraged into academics by my late cousin and adviser Prof. Tony Adegbola (alias uncle say bros), former Deputy Vice-Chancellor, University of Ife. "All flesh is Grass" was the topic of his Inaugural lecture. His flesh became Grass in September 1997. May his kind soul continue to rest in Peace.

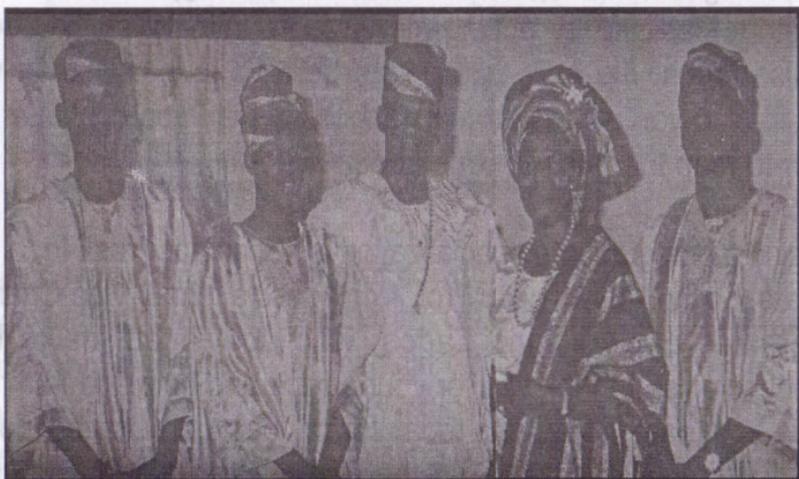
Maybe I would not have finished the medical course having been fed up in my second year, by the overdose of Biochemistry lectures and practicals but for a young couple, then my lecturers – Adeyemo and Oyinate Elebute who persuaded me to bear with Biochemistry for another year so that I could move into the more interesting clinical years. Later as Prof. and Prof. (Mrs) Elebute, they continued to be my academic advisers for a long time. Prof. (Mr), an international Cardiothoracic Surgeon, vetted my early papers until I found my feet in paper writing. Prof. (Mrs), a Professor of Physiology, introduced me to Laboratory Medicine by putting me through animals' study research. She also taught me how to combine being a career woman with a family life. To you wonderful teachers, I say may you continue to live forever to reap the fruits of your labour.

Choosing a postgraduate specialization is not an easy task for a young graduate. So, my thanks go to Prof. Akin Adesola former Vice-Chancellor Universities of Ilorin and Lagos, who convinced me to be an Ophthalmologist. I thank you for your advice and help and I am happy that we both have no regrets today for my being an Ophthalmologist. When I was invited to take up the Secretaryship of the Faculty of Ophthalmology, National Postgraduate Medical College of Nigeria, little

did I envisage that one day, I would be the Millennium President of the College and one day confer an Honorary Fellowship of the college on the President of the Nation. For this, my appreciation goes to Prof. Theo Ogunlesi, my maternal cousin and Professor Emeritus University of Ibadan. Thank you Sir, for your continuous support at all time, and for your confidence in me.

My mentors in Ophthalmology are Mr. Alan Friedmann, Mr. Giftie Munton, Prof. Desmond Archer formerly head of the Department of Ophthalmology, Queen's University of Belfast Ireland, Mr. Vincent Marmion of the Royal Eye Hospital Bristol, and lately Prof. Ian Grierson, Littlewood Professor and Head, Experimental Ophthalmology unit, The University of Liverpool. I thank you all for giving me the encouragement, support and opportunity to be and remain an academic ophthalmologist. I am indeed grateful.

To my nuclear family – the boys – Sunday, Afolabi, Akintoye and Olajide, I thank you for giving me the push and support at all time. “Mummy can do it” is what I hear most of the time. I am grateful to you for being my advisers and I.T. instructors. My daughter, Princess Abiola must not be left out. She is my daughter indeed and not my daughter-in-law. She came and filled the gap that was left in the family. God bless you.



Prof. Majekodunmi and her family

I am particularly grateful and feel fulfilled that Afolabi and Olayinka Shoneye-Vaughan, my nephew, have taken the baton to be Ophthalmologists – to God be the Glory.

Engineer Olayiwola Adegbola, my brother, pillar of support, economic adviser & master planner, I appreciate all your help and care. May God continue to care for you . To my late sister Mrs. Adeola Ibirogba, I wish you were here to take your own share of the glory of my success but God knows best. “Obiren meta” rest in Perfect Peace.

To my numerous patients, without whom I will not be here to give this lecture, I say well done. May God continue to give you good Sight. To my colleagues in the Ophthalmology Unit, especially my academic children Drs. Folasade Akinsola, Adeola Onakoya and Fisayo Aribaba, my past and present residents and nursing staff at the Guinness Eye Centre, I say God bless you. I promised earlier in my career to train Ophthalmologists not only for civilians but also for uniformed sector. Up to date, I have trained Ophthalmologists for the Military, Navy, Air Force and Police!



Prof. Majekodunmi in the middle with her consultants and residents



Prof. Majekodunmi (middle) with her past residents and Matrons Adedoyin (right) and Sodeinde (standing 4th left) at the Guinness Eye Centre LUTH, Idi-Araba

I thank you all for accepting and cooperating with my leadership.

My secretaries over the years have all been dedicated and committed. They were all God sent and I count myself lucky to have had this crop of faithful servants whom I can now look upon as my extended family. Mrs. Folake Adeniyi, Mr. Ramoni Morakinyo, Mrs. Gladys, Mrs. Grace John and currently Mrs. Eno Attai and Mrs. Eunice Momoh. To you all I say thank you. Mrs. Rashidat Tanimola, the computer guru gave the I.T. assistance, and Mr. Dalegan of Medical Illustration Department CMUL was helpful. You are both hereby acknowledged.

Soon I shall be leaving the Arena, but my mind is at peace that I have trained successors who will keep the flag flying.

My appreciation goes to the Head of Senate and Ceremonies Unit, Mr. David Kalu, Ag. Managing Director, University of Lagos Press Mrs. B.A. Awere and Mr. Adetunji and the entire staff of the Press, the Work and Services personnel, the CET and the Security Unit of the University for all their technical and editorial support.

I am indeed grateful.

Finally, to the University of Lagos, CMUL and Lagos University Teaching Hospital, the sister institution where I started my training, graduated, had my “freedom” and spent my working life, I am grateful for the opportunities given me and for making it possible for me to pay this debt – the Inaugural lecture which I give today.

Mr. Vice-Chancellor Sir, Ladies & Gentlemen all other protocols observed, in ending this lecture, permit me to quote an unknown author and I quote.

“THE GREAT USE OF LIFE IS TO SPEND IT FOR SOMETHING THAT WILL OUT LAST IT. AND THE JOY OF EXISTENCE LIES ON ACHIEVEMENT AND RECOGNITION”. HISTORY WILL TELL WHETHER MY LIFE HAS BEEN ALL THESE, AND MORE.

DISTINGUISHED LADIES & GENTLEMEN I THANK YOU ALL FOR YOUR ATTENTION AND GOD BLESS.

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