TOPIC:

WHAT CONCERNS THE DENTIST WITH TUMOURS AND HOSPITAL MANAGEMENT?

By

PROFESSOR ONATOLU ODUKOYA
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By

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INTRODUCTION
The DENTIST or the DENTAL SURGEON is the health professional entrusted with the responsibility of managing the teeth and its immediate environment in health and disease. The immediate environment could be the gum (gingiva), the palate (the hard and soft parts), the tongue, the floor of the mouth, the cheeks (buccal mucosa) and the lips. By extension, the upper and the lower jaws, and the face. The profession is simply referred to as DENTISTRY or DENTAL SURGERY.

A minimum of credit in Physics, Chemistry and Biology as well as Mathematics and English at the School Certificate level, good score in JAMB and Post JAMB screening are the prequalification for admission into the undergraduate training in Dentistry, that leads to award of the Bachelor of Dental Surgery (B.D.S.) degree of the University of Lagos. The undergraduate dental programme lasts for 12 Semesters during which students are exposed to Basic and Clinical Medical Sciences as well as Basic and Clinical Dental Sciences.

A graduate Dentist could proceed to specialise in any of the following Dental Specialties after one year Housemanship and one year National Youth Service Corps programme:
- Oral Pathology (Oral & Maxillofacial Pathology)
- Oral Surgery (Oral & Maxillofacial Surgery)
- Paedodontics (Paediatric Dentistry)
- Orthodontics
- Conservative Dentistry
- Prosthetic Dentistry
- Oral Medicine
- Periodontology
- Oral Diagnosis & Radiology
- Community Dentistry

A) THE SIGNIFICANCE OF THE MOUTH
The mouth starts playing a significant role in the life of a human being from the very moment the child is born. One of the initial
role performed is crying, an emotion expressed through the mouth. The infant being has been described as “a MOUTH with a body attached, and development can be related to five subphases of orality: sucking, mouthing, biting, chewing and swallowing.

As the baby develops further into childhood, and milk teeth that had been cut are lost and replaced by permanent teeth, some of the personality of the growing child starts to change. The desire to eat with adults on the dining table is developed as early as the milk teeth start appearing in the mouth. Dietary changes are noticed.

The mouth is a strong tool for communication both in infancy, childhood, adolescence and adulthood. Beside talking through the mouth, emotions are also expressed through the mouth. The shape of the mouth expresses joy by smiling and raising the corners of the mouth or depression by dropping the corners of the mouth.

The appearance of an individual is further expressed through well-set teeth and beautifully shaped lips. For this reason, artists and other public figures are more concerned with their mouth. In order to enhance their appearance, ladies apply different colours of lipstick to the vermillion border of the lips.

The lips and the tongue also play an important role as sexual organs in both female and males. This is effected through kissing. A clean mouth with strong white teeth is an indication of a healthy individual.

B) THE MOUTH IN DISEASE STATE

Disease of the mouth may arise from tissues that are native to the mouth. However, diseases that affect other systems of the body may also manifest in the mouth. Whenever the mouth is in a disease state, some or all the functions that make the mouth significant are compromised.

The following diseases may arise from tissues native to the mouth and the jaws:

a) Developmental Disorders
i) Developmental disorders of the teeth
   Examples of which are: Microdontia, Macroodontia, Partial or Total Anodontia, Supernumerary teeth, Premature Eruption, Delayed Eruption, Impacted Teeth, Dilaceration, Taurodontism, Gemination, Fusion, Hypercementosis, Amelogenesis Imperfecta, Dentinogenesis Imperfecta.

ii) Developmental disorders of oral soft tissues
   Examples of which are: Congenital Lip Pits, Double Lips Ankyloglossia, Macroglossia, Fordyce Granules.

iii) Developmental disorders affecting the jaw bones
   Examples of which are: Hemifacial Hypertrophy, Hemifacial Atrophy, Cleft Lip, Cleft Palate, Cleidocranial Dysplasia.

b) Cystic Lesions
   Examples of which are: Odontogenic and non odontogenic cysts.

c) Inflammatory Lesions
   This varies from Dental Caries to Pulpitis and Periapical Inflammatory Diseases. Inflammatory diseases of bone such as Osteomyelitis is also an example. Oral soft tissue infections include Bacterial, Viral and Mycotic (Fungal) infections.

d) Traumatic Injuries
   This varies from simple trauma to the teeth, especially the upper anterior teeth, resulting in fracture of the affected teeth.
Trauma to the face and oral regions may also result in fracture of the facial and jaw bones.

e) Tumours
Tumour refers simply to swelling. However, long historic precedent has equated the term Tumour with Neoplasm, while the other usages of tumour as one of the cardinal signs of inflammation has now passed into limbo.

Neoplasm, which simply put is ‘new growth’ has been better defined by Willis as ‘an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoke the change’. Neoplasia could be Benign or Malignant.

i) Broad classification of oral tumours (neoplasia)
The presence of teeth in the mouth makes the mouth unique, when compared with other structures in the body. Development of the tooth is complex and unique as well. Other structures in the mouth such as mucosa, bone, muscular organ (the tongue) and glandular tissues are similar to other structures elsewhere in the body. For this reason, oral tumours can be simply classified into the following two categories namely:

ODONTOGENIC TUMOURS (on the basis of their development from the tooth or its primordium) and NON ODONTOGENIC TUMOURS (on the basis of their development from other structures beside the tooth and its primordium).

The following are examples of Odontogenic Tumours:

BENIGN TUMOURS
Epithelial Odontogenic Tumours
Ameloblastoma
Calcifying Epithelial Odontogenic Tumour
Adenomatoid Odontogenic Tumour

MALIGNANT TUMOURS
Malignant Ameloblastoma
Ameloblastic Fibroma
Odontoma
Ameloblastic Fibro-Odontoma

Calcifying Odontogenic Cyst
Squamous Odontogenic Tumour
Mesenchymal Odontogenic Tumours
Odontogenic Fibroma
Odontogenic Myxoma
Cementoblastoma
Mixed Odontogenic Tumours
Ameloblastic Fibroma
Odontoma
Ameloblastic Fibro-Odontoma

MALIGNANT TUMOURS
Malignant Ameloblastoma
Ameloblastic Carcinoma
Odontogenic Carcinoma
Primary Intraosseous Carcinoma
Ameloblastic Fibrosarcoma
Odontogenic Carcinosarcoma

The following are examples of Non Odontogenic Tumours:

Epithelial Tumours
Benign
Papilloma
Naevus
Malignant
Squamous Cell Carcinoma
Melanoma

Connective Tissue Tumours
Benign
Fibroma
Neurofibroma
Lipoma
Neurilemoma
Leiomyoma
Rhabdomyoma
Hemangioma
Lymphangioma
Malignant
Fibrosarcoma
Neurogenic sarcoma
Liposarcoma
Neurogenic Sarcoma
Leiomyosarcoma
Rhabdomyosarcoma
Angiosarcoma, Kaposi’s Sarcoma
Angiosarcoma, Kaposi’s Sarcoma
Burkitt Lymphoma
Non-Hodgkin’s Lymphoma
Hodgkin’s Lymphoma
Bone Tumours

Benign

- Osteoma
- Osteoid Osteoma
- Osteoblastoma
- Cemento-Ossifying Fibroma
- Central Giant Cell Lesion
- Osteochondroma

Malignant

- Osteogenic Sarcoma
- Chondrosarcoma

C). GENERAL COMMENTS ON ORAL TUMOURS

Oral tumours, especially the benign ones, present as intraoral swellings which may or may not cause discomfort to the patient. Some benign tumours, such as Ameloblastoma, may produce discomfort and extroral swelling which affects the aesthetics of the patient. The malignant tumours, on the other hand, tend to grow bigger, may be ulcerated, and may even extend beyond the primary site located and the nasal cavity. Malignant lesions, even extended to locations far away from the oral cavity, are worth noting that malignant lesions located far away from the mouth, such as the lung, the kidney, the prostate, the ovaries and testis may also send metastases to the oral cavity.

D). WHICH ORAL TUMOURS HAVE ATTRACTED THE INTEREST OF THE AUTHOR?

I have been attracted to the following two types of oral tumours:

a) Oral Cancer with particular emphasis on Squamous Cell Carcinoma.

b) Odontogenic Tumours with emphasis on Ameloblastoma

E). HOW DID THE AUTHOR BECOME INTERESTED IN ORAL TUMOURS AS AN AREA OF CONCENTRATION?

I was privileged to attend the Harvard School of Dental Medicine, Boston, Massachusetts, United States of America (from July 1980 to April 1984) for my postdoctoral program in Oral Pathology under the Chairmanship of Professor Gerald Shklar, whose research interest focused on Experimental Oral Carcinogenesis, using the Hamster Buccal Pouch Animal Model. The experience I had, interacting with Professor Gerald Shklar, motivated and encouraged me to be interested in research on oral squamous cell carcinoma.

Having acquired research skill during my training abroad, I therefore would need that I apply some of the research skill that I have acquired to investigate this tumour. This explains my interest in this tumour as well.

2. THE AUTHOR'S CONTRIBUTIONS TO RESEARCH ON ORAL SQUAMOUS CELL CARCINOMA

Animal models for studying oral diseases have been in existence. My research career in experimental study of Oral Squamous Cell Carcinoma started with the use of the Syrian Hamster Buccal Pouch Carcinoma model.

The Syrian hamster buccal pouch model was induced with 7, 12 Dimethyl Benz(a) Anthracene (DMBA), and the hamster buccal pouch by painting DMBA on the buccal pouch of the animal. The hamster buccal pouch is similar to the keratinizing human oral mucosa in its histology, histochemistry, and ultrastructure. Furthermore, success of carcinosarcoma induction is to 12 weeks of treatment of the animal with DMBA involved. There is consistency in patterns of tumour development, in which leukoplakia precedes frank epidermoid carcinoma, which is observable within 10 weeks of treatment of the animal with DMBA. This model, in which oral squamous cell carcinoma was induced, proved to be the best because of the following advantages it possesses:

a) The hamster buccal pouch has been considered the best because of the following advantages it possesses:

i. There is consistency in patterns of tumour development, in which leukoplakia precedes frank epidermoid carcinoma, which is observable within 10 weeks of treatment of the animal with DMBA.

ii. The Syrian hamster is similar to the human in its histology, histochemistry, and ultrastructure.

iii. The success of carcinosarcoma induction is 100%.

iv. The hamster buccal pouch is similar to the keratinizing human oral mucosa in its histology, histochemistry, and ultrastructure.

Of all animal models of oral carcinosarcoma, the hamster buccal pouch model has been considered the best because of the following advantages it possesses:

a) The hamster buccal pouch model has been considered the best because of the following advantages it possesses:

i. There is consistency in patterns of tumour development, in which leukoplakia precedes frank epidermoid carcinoma, which is observable within 10 weeks of treatment of the animal with DMBA.

ii. The Syrian hamster is similar to the human in its histology, histochemistry, and ultrastructure.

iii. The success of carcinosarcoma induction is 100%.

iv. The hamster buccal pouch is similar to the keratinizing human oral mucosa in its histology, histochemistry, and ultrastructure.
c) The model is susceptible to systemic influences such as drugs, hormones, and immunologic influences.
d) Spontaneous tumours do not occur in the hamster buccal pouch model.

A. TWO-PHASE CARCINOGENESIS IN HAMSTER BUCCAL POUCH (Odukoya & Shklar, 1982)
In this study, 60 male and female young adult golden Syrian hamsters (Mesocricetus auratus) were divided into the following 3 equal groups of 10 males and 10 females:
a) Group 1: 0.1% DMBA in heavy mineral oil painted thrice weekly on to the left buccal pouch of the hamsters for 10 weeks. No treatment for the next 10 weeks.
b) Group 2: Painting with 0.1% DMBA for 10 weeks. No painting for 6 weeks. Painting with 0.5% DMBA in mineral oil for 4 weeks (from week 16 to week 20).
c) Group 3: No painting for 15 weeks. Painting with 0.5% DMBA in mineral oil from week 16 to week 20.

Result
a) Group 1: No tumour.
b) Group 2: White lesions and tumours in buccal pouches of all animals. Tumours were microscopically interpreted as squamous cell carcinoma.
c) Group 3: Inflammation. No tumour.

Conclusion
Low dosage carcinogen (0.1% DMBA) applied for 10 weeks did not cause cancer in the animals. At this stage, cells predetermined to form cancer may have been formed but not visible macroscopically. The altered cells remain so for another six weeks when animals were not treated. Subsequent treatment from week 16 to week 20 with a higher dose carcinogen (0.5% DMBA) resulted in development of cancer. This study established a concept that carcinogenesis could be in 2 phases, although carcinogen was used in both the 1st and the 2nd phases.

B. INITIATION AND PROMOTION IN EXPERIMENTAL ORAL CARCINOGENESIS (Odukoya & Shklar, 1984)
In this study, 66 adult male and female golden Syrian hamsters were divided into the following six groups:
a) Group 1 (8 males, 8 females): Painting of buccal pouches with 0.1% DMBA for 10 weeks. No painting for 12 weeks.
b) Group 2 (8 males, 8 females): Painting with 0.1% DMBA for 10 weeks. No treatment for 6 weeks. Painting with 40% Benzoyl Peroxide in acetone from week 17 to week 22.
c) Group 3 (8 males, 8 females): Painting with 0.1% DMBA for 10 weeks. No treatment for 6 weeks. Painting with acetone from week 17 to week 22.
d) Group 4 (3 males, 3 females): No painting for 16 weeks. Painting with 40% Benzoyl Peroxide in acetone from week 17 to week 22.
e) Group 5 (3 males, 3 females): No painting for 16 weeks. Painting with Acetone from week 17 to week 22.
f) Group 6 (3 males, 3 females): No painting from week 1 to week 22.

Result
a) Group 1: No tumour.
b) Group 2: Leukoplakia and tumours, microscopically interpreted as squamous cell carcinoma.
c) Group 3: No tumour.
d) Group 4: No tumour.
e) Group 5: No tumour.
f) Group 6: No tumour.

Interpretation of result
0.1% DMBA in mineral oil applied to the hamster buccal pouch for 10 weeks did not result in tumour formation in any of the groups.
No tumour was observed 6 weeks (and even beyond) after cessation of DMBA painting, as demonstrated in Group 1 animals.
Application of 40% Benzoyl Peroxide in Acetone for 6 weeks, after waiting for 6 weeks following cessation of carcinogen application, as demonstrated in Group 2 animals resulted in development of Squamous cell carcinoma.

Application of Acetone alone in place of 40% Benzoyl Peroxide in Acetone, as demonstrated in Group 3 animals yielded no tumour.

Application of 40% Benzoyl Peroxide in acetone or Acetone alone, without the initial application of carcinogen as demonstrated in Groups 4 and Group 5 did not yield tumour.

Conclusion
0.1% DMBA in mineral oil served as tumour initiator while 40% Benzoyl Peroxide in Acetone served as tumour promotor, in line with original concept demonstrated in mouse skin by Berenblum and Shubik in 1947. This study was the first that demonstrated the concept of initiation and promotion in oral carcinogenesis.

C. ORAL MUCOSAL TUMOURS INHIBITION BY IBUPROFEN(Cornwall, Odukoya & Shklar, 1983)
In this study, 80 young male and female golden Syrian hamsters were divided into the following 4 equal groups:

Group 1(10 males, 10 females): 0.1% DMBA in heavy mineral oil painted thrice a week onto left buccal pouches of hamsters for 24 weeks.

Group 2(10 males, 10 females): 0.1% DMBA applied as above for 24 weeks. 10 mg. Ibuprofen in aqueous suspension administered orally twice a week for the same 24 weeks.

Group 3(10 males, 10 females): 10 mg. Ibuprofen in aqueous suspension administered twice weekly for 24 weeks.

Group 4(10 males, 10 females): Untreated controls.

2 male and 2 female animals from each group were randomly selected, killed and the buccal pouches examined for presence of tumour at weeks 25, 26, 27, 28 and 29.

Result

<table>
<thead>
<tr>
<th>Group</th>
<th>Average size of tumours (in mm) at animal sacrifice</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wk 25</td>
</tr>
<tr>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Interpretation of result
Group 1 animals developed a statistically significant higher average size of tumours than Group 2 animals, suggesting that Ibuprofen significantly delayed tumour formation in this experiment. In this experiment, ibuprofen, a non steroidal anti-inflammatory agent, acted as a prostaglandin inhibitor. Prostaglandin has been documented to enhance induction of squamous cell carcinoma in experimental animals (Lupulescu, 1978, 1980).

D. RETARDATION OF EXPERIMENTAL ORAL CANCER BY TOPICAL VITAMIN E(Odukoya, Hawach & Shklar, 1984)
In this experiment, 48 male and female golden Syrian hamsters (Mesocricetus auratus) were divided into 4 groups of 12 animals per group as follows:

Group 1: 0.5% DMBA in heavy mineral oil was painted to the left buccal pouches of animals thrice a week for 7 weeks.

Group 2: 0.5% DMBA treatment as above. Painting of 47.5 mg Vitamin E to left buccal pouches of animals thrice a week for 4 weeks after cessation of DMBA painting.

Group 3: No treatment for 7 weeks. Painting with vitamin E as above from week 8 to week 11.

Group 4: No treatment for 11 weeks.
At the end of 11th week, 6 animals in each group were killed and the left buccal pouches examined for presence of tumours. The remaining 6 animals in each group were killed at the end of the 12th week.

Result

Tumours (microscopically interpreted as squamous cell carcinoma) were observed in Groups 1 and 2 animals. No tumours were seen in Groups 3 and 4 animals. Analysis of tumour formation in Groups 1 and 2 animals is given below:

<table>
<thead>
<tr>
<th>Tumour formation</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of tumours</td>
<td>54</td>
<td>30</td>
</tr>
<tr>
<td>Average no. of tumours at 11th week</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Average tumour size</td>
<td>3mm</td>
<td>2mm</td>
</tr>
<tr>
<td>Average no. of tumours at 12th week</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Average tumour size</td>
<td>4mm</td>
<td>2.5mm</td>
</tr>
<tr>
<td>Mean no. of tumours/animal</td>
<td>4.53 ± 1.19</td>
<td>2.50 ± 0.90</td>
</tr>
</tbody>
</table>

Group 1 vs. Group 2 p<0.01

Interpretation of Result

The result showed that Vitamin E applied topically to the hamster buccal pouch for 4 weeks following 7 weeks of DMBA application significantly inhibited tumour formation. It is suggested that the mechanism of action of Vitamin E is that it played a role as an antioxidant, preventing oxidation of the DMBA to diol-epoxide, which is the ultimate carcinogen that caused induction of tumours in this experiment.
Result
Density and Distribution of Langerhans Cells in Epidermal whole mounts treated with Vitamin E and Vitamin E + DMBA

<table>
<thead>
<tr>
<th>Group</th>
<th>A(mo)</th>
<th>B(vit. E)</th>
<th>C(dmba)</th>
<th>D(dmba+vit E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Animals</td>
<td>6</td>
<td>9</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>No. of Langerhans cells</td>
<td>613.8±186.8</td>
<td>347.8±38.3</td>
<td>90.1±13.59</td>
<td>207.1±53.15</td>
</tr>
<tr>
<td>No. of foci</td>
<td>450.1±47.2</td>
<td>67.6±12.7</td>
<td>51.3±20.4</td>
<td>21.8±15.9</td>
</tr>
<tr>
<td>No. cells/foci</td>
<td>567.0±72.6</td>
<td>503.8±17.1</td>
<td>50.8±6.4</td>
<td>194.0±52.6</td>
</tr>
</tbody>
</table>

Bonferonni analysis was applied as follows:

<table>
<thead>
<tr>
<th>VITAMIN E</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>YES</td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

Level of significance is at P value ≤ 0.05/6 = 0.0083.
Means compared were A vs B, C vs D, A vs C, B vs D, A vs D and B vs C.
With respect to the number of Langerhans cells, Mean scores in all groups compared were statistically significant (p ≤ 0.0083) except for groups A vs B which was not statistically significant (p ≥ 0.0083).
With respect to number of foci, Mean scores in all groups compared were statistically significant (p ≤ 0.0083) except for groups B vs C.

Conclusion
Density of Langerhans cells decreased following treatment with DMBA, and the decrease was much less when vitamin E was applied in combination with DMBA.

Langerhans cells are macrophage equivalent cells found in skin and oral mucosa and have been shown to play a role in immune functions. Therefore, vitamin E may retard experimental oral carcinogenesis by maintaining number of Langerhans cells, thereby enhancing immunity of the host.

F. AN EPIDERMED CARCINOMA CELL LINE DERIVED FROM HAMSTER 7,12-DIMETHYL BENZ (a) ANTHRACENE-INDUCED BUCAL POUCH TUMOURS (Odukoya et al, 1983)

In this study, epidermoid carcinoma induced in the hamster cheek pouch with thrice weekly application of 0.5% DMBA in mineral oil for 12 weeks, was excised and processed for in vitro cultivation in culture media consisting of Dulbecco's Minimum Essential Media (DMEM) supplemented with 10% Fetal Bovine Serum (FBS), 100 IU penicillin/ml, 100 μg streptomycin /ml, 10 μg hydrocortisone /ml, 10 μg amphotericin B/ml and 50ng epidermal growth factor (EGF)/ml. The cells were incubated in a humidified atmosphere of 5% CO₂ and 95% air at a temperature of 37° C. After a successful growth in primary culture, the cells were subsequently cultured in a culture media consisting of DMEM, supplemented with 10% FBS, 50ng EGF/ml and 100 μg gentamycin/ml. The cells were incubated in a humidified atmosphere of 5% CO₂ and 95% air at a temperature of 37° C. The successfully cultured cells, which had developed into a cell line, were named Hamster Cheek Pouch Carcinoma-1 (HCPC-1) cell line, and had been maintained for 60 passages over a period of 15 months.
The cell line was demonstrated to have the following characteristics:

i) Population doubling time of 12 hours, estimated from the exponential phase of the growth curve established for the cell line.

ii) Plating efficiency of 35% estimated from proportion of colonies formed relative to number of seeded cells, two weeks after seeding of 50 and 500 cells.

iii) Ultrastructural demonstration of desmosomes and tonofilaments in cells, thereby confirming the epithelial nature of the HCPC 1 cells.

iv) Histochemical demonstration of keratin in the cytoplasm of the cells by staining with rhodanile blue stain.

v) Immunological localization of keratin in HCPC 1 cells by indirect immunofluorescence method, in which cells were primarily treated with rabbit anti human keratin antibody, and further treated with fluorescein labelled goat anti rabbit IgG. The final reaction was examined under the light microscope with fluorescent attachment.

vi) Successful transplantation of HCPC 1 to cheek pouches of hamsters gave rise to tumours microscopically interpreted as different types of epidermoid carcinoma as presented in the following table:

<table>
<thead>
<tr>
<th>TRANSPLANTATION STUDY WITH HCPC-1 CELLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation size</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>2.4 x 10^4</td>
</tr>
<tr>
<td>1.8 x 10^5</td>
</tr>
<tr>
<td>1 x 10^6</td>
</tr>
</tbody>
</table>

Conclusion

This is the first study in the scientific literature, where DMBA induced hamster cheek pouch epidermoid carcinoma has been successfully cultured. The HCPC 1 cell line has opened avenue for studies on molecular biology of DMBA induced epidermoid carcinoma of the hamster cheek pouch. In fact, many of such studies that emanated from the laboratory where we carried out our work, have been published in international journals.

G VITAMIN E STIMULATES PROLIFERATION OF EXPERIMENTAL ORAL CARCINOMA CELLS IN VITRO (Odukoya et al, 1986)

In this study, HCPC 1 cells were propagated in Eagle's minimum essential medium (EMEM) supplemented with 10% fetal calf serum (FCS), 19µg gentamycin/ml, and incubated in a humidified atmosphere of 5% CO₂, and 95% air at a temperature of 37°C. The following 2 experiments were set up:

Experiment 1:

HCPC 1 cells numbering 100 cells/culture were propagated in culture media containing the following concentrations of Vitamin E: 0.1, 1.0, 10, and 100 µM. The vitamin E dilutions were made up in 100% absolute ethyl alcohol before they were introduced into the cultures. Control cultures containing 100% absolute ethyl alcohol were also set up. The cultures were terminated 10 days after they were set up, the cells were stained with crystal violet, colonies formed / culture were observed, counted and recorded.

Experiment 2:

HCPC 1 cultures containing 10⁵ cells/culture were set up. 24 hours following seeding of cells, the normal media were replaced with culture media containing the following dilutions of Vitamin E: 0.1, 1.0, 10 and 100 µM. Control cultures with 100% absolute ethyl alcohol and untreated cultures were also set up. 24 hours after treatment of cultures with Vitamin E (Day 2), half the number
of experimental and control cultures were retrieved, and the cells were counted. On Day 4, the remaining cultures were also retrieved and the cells counted.

The results of experiments 1 and 2 were analysed statistically, using the student’s t test for comparison of paired means.

Result

1) **Effect of Vitamin E on Colony formation by HCPC 1 Cells**

<table>
<thead>
<tr>
<th>Vitamin E conc. (µM)</th>
<th>Average No. (± SD) of colonies</th>
<th>Average Plating Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>48±1.0</td>
<td>48%</td>
</tr>
<tr>
<td>0.1</td>
<td>58.3±4.8</td>
<td>58.3%</td>
</tr>
<tr>
<td>1.0</td>
<td>64.3±3.4</td>
<td>64.3%</td>
</tr>
<tr>
<td>10.0</td>
<td>68±2.6</td>
<td>68%</td>
</tr>
<tr>
<td>100.0</td>
<td>41.7±3.5</td>
<td>41.7%</td>
</tr>
</tbody>
</table>

There was a statistically significant increase in number of colonies formed with increasing concentration of Vitamin E up to 10 µM (p ≤ 0.05). The number of colonies formed decreased at 100 µM.

2) **Effect of Vitamin E on cell turnover of HCPC 1 cells**

<table>
<thead>
<tr>
<th>Vitamin E Conc. (µM)</th>
<th>Day 2 Mean cell no. (± SD) x 10^5</th>
<th>Day 4 Mean cell no. (± SD) x 10^5</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9±0.16</td>
<td>21.3±9.5</td>
</tr>
<tr>
<td>0.1</td>
<td>2.1±0.26</td>
<td>25.3±9.5</td>
</tr>
<tr>
<td>1.0</td>
<td>2.6±0.16</td>
<td>30.0±10.0</td>
</tr>
<tr>
<td>10.0</td>
<td>1.3±0.21</td>
<td>15.0±3.1</td>
</tr>
<tr>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was a statistically significant increase in cell number (p ≤ 0.001) with increasing concentration of Vitamin E in the culture media up to 10 µM on both Day 2 and Day 4. The number of cells counted on both days decreased at Vitamin E dilution of 100 µM.

**Conclusion**

Vitamin E stimulated colony formation and cell turnover of HCPC 1 at low concentrations up to 10 µM. Antioxidant property of Vitamin E in which it served as free radical scavenger was responsible for this action. At a dilution of 100 µM, Vitamin E was cytotoxic to HCPC 1 cells. Vitamin E’s property as a surfactant, which makes it act as a non ionic detergent may explain this action. Action of Vitamin E in vivo where it inhibits tumour formation could be a combination of its antioxidant property and immune enhancing property as already demonstrated in previous studies. In the in vitro system presented in this study, the immune enhancing function was absent.

H. THE EFFECT OF AFB ON THE DEVELOPMENT OF MOPHOLIGIC DYSPLASIA IN DMBA CARCINOGENESIS OF THE RAT PALATAL EPITHELIUM (Odukoya et al, 1990)

In this study, 48 Sprague-Dawley rats were divided into the following 8 groups of 6 animals per group:

- **Group 1:** 0.5% DMBA solution in liquid paraffin was painted thrice weekly for 30 weeks on the palate of desalivated animals (animals were desalivated by subcutaneous injection of methyl scopolamine, 1 mg per kg body weight).
- **Group 2:** DMBA was applied as above + Aflatoxin B, 4 µg/ml in groundnut oil (oral administration) for 14 weeks.
- **Group 3:** DMBA was applied as above + Aflatoxin B, 10 µg/ml in groundnut oil applied as in group 2.
- **Group 4:** Liquid paraffin was painted in a similar way that DMBA was painted in group 1.
- **Group 5:** Aflatoxin B, 4 µg/ml was administered as in group 2.
- **Group 6:** Aflatoxin B, 10 µg/ml was administered as in group 3.
- **Group 7:** Groundnut oil applied as vehicular control for Aflatoxin B1.
- **Group 8:** Untreated control.

**Conclusion**

Vitamin E stimulated colony formation and cell turnover of HCPC 1 at low concentrations up to 10 µM. Antioxidant property of Vitamin E in which it served as free radical scavenger was responsible for this action. At a dilution of 100 µM, Vitamin E was cytotoxic to HCPC 1 cells. Vitamin E’s property as a surfactant, which makes it act as a non ionic detergent may explain this action. Action of Vitamin E in vivo where it inhibits tumour formation could be a combination of its antioxidant property and immune enhancing property as already demonstrated in previous studies. In the in vitro system presented in this study, the immune enhancing function was absent.
Three animals from each of the groups were killed with ether at 14 weeks and 30 weeks. Palatal mucosa of each rat was removed and processed for microscopic examination for development of morphologic dysplasia.

**Result**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD epithelial dysplasia score 14 weeks</th>
<th>Mean ± SD epithelial dysplasia score 30 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.33±0.58</td>
<td>2.00±0.00</td>
</tr>
<tr>
<td>2</td>
<td>2.00±0.00</td>
<td>3.00±0.00</td>
</tr>
<tr>
<td>3</td>
<td>2.00±0.00</td>
<td>3.30±0.00</td>
</tr>
<tr>
<td>4</td>
<td>2.33±0.58</td>
<td>3.67±0.58</td>
</tr>
<tr>
<td>5</td>
<td>1.00±0.00</td>
<td>1.33±0.58</td>
</tr>
<tr>
<td>6</td>
<td>1.00±0.00</td>
<td>2.00±0.00</td>
</tr>
<tr>
<td>7</td>
<td>1.33±0.58</td>
<td>1.33±0.58</td>
</tr>
<tr>
<td>8</td>
<td>1.00±0.00</td>
<td>1.33±0.58</td>
</tr>
</tbody>
</table>

Mean score of morphologic dysplasia was consistently higher in group 3 animals than group 2, and higher in group 2 than group 1 (p<0.01). ANOVA was the statistical method of analysis applied.

**Conclusion**

Aflatoxin B1, either in low dose of 4 µg/ml or a relatively higher dose of 10 µg/ml augmented development of morphologic dysplasia in DMBA treated desalivated rats. The higher dose of 10 µg/ml was more effective.

Aflatoxin B1 is speculated to act as a cocarcinogen in this experiment.

**I. EFFECT OF ORAL CONTRACEPTIVE ON DMBA CARCINOGENESIS OF THE RAT PALATAL MUCOSA (Allen, Odukoya and Ashiru, 1990)**

In this study, 40 weaners female Sprague-Dawley rats were divided into the following 8 groups of 5 animals per group:

- **Group 1**: 0.5% DMBA in liquid paraffin was painted thrice weekly on to the palate of desalivated rats for 18 weeks.
- **Group 2**: DMBA as in group 1 + Oral contraceptive 1 (Norethindrone, 13.0 gm% + Ethyl oestradiol, 8.7 mg%, both in corn oil) administered through nasogastric tube for 18 weeks.
- **Group 3**: DMBA as in group 1 + Oral contraceptive 2 (Norethindrone, 6.5 gm% + Ethyl oestradiol, 4.35 mg%, in corn oil) administered through nasogastric tube for 18 weeks.
- **Group 4**: Oral contraceptive 1 administered for 18 weeks.
- **Group 5**: Oral contraceptive 2 administered for 18 weeks.
- **Group 6**: Liquid paraffin (vehicle control for DMBA) painted thrice weekly on to the palate of desalivated rats for 18 weeks.
- **Group 7**: Oral contraceptive 1 administered via nasogastric tube for 18 weeks.
- **Group 8**: Untreated control.

All animals were killed with ether at 18 weeks, their palatal mucosa removed and processed for microscopic evaluation of epithelial dysplasia. Furthermore, morphometric analysis was performed on epithelial and keratin thickness of each palatal mucosal specimen.

**Result**

**Distribution of mean scores of epithelial dysplasia among groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean score ± SD of epithelial dysplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.2±0.4</td>
</tr>
<tr>
<td>2</td>
<td>2.6±0.49</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>4</td>
<td>1.67±0.94</td>
</tr>
<tr>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>7</td>
<td>1.0</td>
</tr>
<tr>
<td>8</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Statistical analysis, using the student's t test was significant only when group 2 was compared with group 1.
Distribution of mean thickness scores of epithelium and keratin layer of epithelium among groups.

Group | Mean thickness scores in μ ± SD |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratin</td>
<td>Epithelium</td>
</tr>
<tr>
<td>1</td>
<td>40.23 ± 1.22</td>
</tr>
<tr>
<td>2</td>
<td>53.37 ± 9.6</td>
</tr>
<tr>
<td>3</td>
<td>25.3 ± 2.03</td>
</tr>
<tr>
<td>4</td>
<td>44.51 ± 4.34</td>
</tr>
<tr>
<td>5</td>
<td>27.25 ± 0.90</td>
</tr>
<tr>
<td>6</td>
<td>111.43 ± 5.07</td>
</tr>
<tr>
<td>7</td>
<td>66.85 ± 5.40</td>
</tr>
<tr>
<td>8</td>
<td>63.52 ± 0.32</td>
</tr>
</tbody>
</table>

Keratin and epithelium thickness scores in group 3 (DMBA + relatively low dose of oral contraceptive) were lower than in group 1 (DMBA). Group 1 scores were lower than group 8 (untreated control) scores.

Conclusion
Relatively high dosage of oral contraceptive augmented morphologic dysplasia induced by DMBA. Relatively low dosage of oral contraceptive augmented epithelial atrophy induced by DMBA.

J. THE IMPLICATIONS OF THE VARIOUS DMBA STUDIES

DMBA (7, 12-Dimethylbenz(a)anthracene) is a synthetic polycyclic aromatic hydrocarbon (PAH) which simulates benzpyrene, a naturally occurring polycyclic aromatic hydrocarbon. Benzpyrene is one of the isolated products of tobacco, and is one of the most carcinogenic naturally occurring PAH. Tobacco has for long been associated with oral cancer.

The various DMBA studies therefore demonstrated indirectly, in the animal model, the effect of tobacco use on oral mucosa, and agents that can modify such effect. Vitamin E and non steroidal anti inflammatory drug such as Ibuprofen slow down oral cancer induced by DMBA, while Aflatoxin B1, a product liberated by fungi following poor food storage, augmented early DMBA carcinogenesis. Oral contraceptive applied to female rats also promoted early DMBA carcinogenesis. These situations are also applicable to human beings. From our presentation so far, we have done more studies on Vitamin E and oral cancer than any other agent that has been studied by us. It is therefore reasonable to suggest that in humans, Vitamin E taken as dietary supplements could reduce risk of developing oral cancer in tobacco users.

In a clinicopathological study of 106 Nigerian cases of oral squamous cell carcinoma by Odukoya et al, 1986, gingiva was the most affected intra oral site, and males were more affected than females. The gingiva, being the most affected site in the Nigerian series is in contrast to observation in the Caucasians, where the lip is the most commonly affected site and the gingiva, one of the least affected site. Both the site issue and the fact that oral squamous cell carcinoma constituted 5.85% of all biopsies in the record of the Department of Oral Pathology and Oral Biology, LUTH, suggest the need to carry out further investigation into the etiology of oral squamous cell carcinoma in Nigerians.

3. SIGNIFICANT CONTRIBUTION TO RESEARCH ON ODONTOGENIC TUMOURS

A. ODONTOGENIC TUMOURS: ANALYSIS OF 289 NIGERIAN CASES (Odukoya, 1995)
Odontogenic tumours have been defined as lesions derived from epithelial or mesenchymal elements or both, that are part of the tooth forming apparatus.

This study was designed to review a relatively larger series (289 cases) of odontogenic tumours over a relatively longer period.
years) from the record of the Department of Oral Biology and Oral Pathology, Lagos University Teaching Hospital. Prior to this study, the most authentic study on epidemiology of Odontogenic Tumours in Nigerians was that reported by Mosadomi (1975), which reviewed 29 cases over a period of 5 years. Furthermore, our series was reviewed in line with the WHO classification of Odontogenic Tumours published in 1992.

Odontogenic tumours constituted 19% of all oral/jaw tumours and tumour-like lesions. Ameloblastoma with a mean age of 31 years was the commonest odontogenic tumour, constituting 58.5% of odontogenic tumours in the series. There was predilection for males and the posterior mandible. There was an overwhelming predominance of benign odontogenic tumours (94.8%) while malignant odontogenic tumours constituted only 5.2% in the series. Odontogenic carcinoma which is generally considered rare, was not that rare in the series, as it constituted 5% of odontogenic tumours. Odontogenic carcinoma in the series occurred at a mean age of 37 years.

### Age Distribution of Histologic Types of Odontogenic Tumours

<table>
<thead>
<tr>
<th>Type of Tumour</th>
<th>No.</th>
<th>Percentage</th>
<th>Mean Age ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign Odontogenic Tumour</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Odontogenic Epithelium without Odontogenic Mesenchyme</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ameloblastoma</td>
<td>169</td>
<td>58.47</td>
<td>31 ±13.8</td>
</tr>
<tr>
<td>Squamous Odontogenic Tumour</td>
<td>3</td>
<td>1.04</td>
<td>40 ±5.0</td>
</tr>
<tr>
<td>Calcifying Epithelial Odontogenic Tumour</td>
<td>1</td>
<td>0.35</td>
<td>21</td>
</tr>
<tr>
<td><strong>Malignant Odontogenic Tumours</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odontogenic Carcinoma</td>
<td>14</td>
<td>4.84</td>
<td>36.8 ±18</td>
</tr>
<tr>
<td>Odontogenic Sarcoma</td>
<td>1</td>
<td>0.35</td>
<td>35</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>289</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

### Conclusion

There is no doubt that odontogenic tumours are not rare among Nigerians. Further studies which will investigate the aetiology and biologic behaviour of Odontogenic tumours are therefore desirable. Findings from such studies will serve as guide to prevention and cure of Odontogenic Tumours.

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**B. LIGHT MICROSCOPIC, CYTOCHEMICAL AND ULTRASTRUCTURAL STUDIES OF RAT ODONTOGENIC EPITHELIAL CELL LINE (Odukoya et al, 1991)**

In an attempt to establish a good in vitro model that should help to study biology of odontogenic tumours, and in realization that odontogenic tumours originate from aberrations and neoplastic transformation of tooth germ, we decided to establish a cell line of odontogenic epithelial cells, derived from tooth germ, which
we believe will be useful in studying the biology of odontogenic epithelial cells and specific tumours, such as Ameloblastoma, that are believed to derive from odontogenic epithelial cells.

Unmineralised maxillary molar tooth germs excavated from the tooth sockets of 11 day old Sprague Dawley albino rats were the source of the odontogenic epithelial cells used in the study.

The tooth germs were digested with 0.25% trypsin and 0.025% collagenase and disaggregated in Medium 199 supplemented with 20% fetal calf serum (FCS). $10^5$ molar germ cells were inoculated with $4 \times 10^5$ mitomycin-C treated 3T3 mouse fibroblasts and were propagated in Medium 199, supplemented with 20% FCS, gentamycin (100 μg/ml), penicillin (1000 i.u/ml), streptomycin (100 μg/ml), amphotericin B (2.5 μg/ml), cholera toxin ($10^{-10}$ M), hydrocortisone (0.4μg/ml) and ascorbic acid (50 μg/ml). They were incubated in a humidified atmosphere of 5% CO$_2$ and 95% air at a temperature of 37°C. Thirty-six hours after primary inoculation, epidermal growth factor (10ng/ml) was added to the culture.

After successful primary culture, the odontogenic epithelial cells were isolated and subcultured on a feeder layer of mitomycin-C treated 3T3 mouse fibroblasts, in a similar culture conditions as for the primary culture. The cell line so established was named ROE-2B (Rat Odontogenic Epithelial cell line). The cells were maintained over a period of 6 months through 7 passages. The odontogenic epithelial cell line has been characterized as follows:

a) 6th passage ROE-2B cells stained with haematoxylin and eosin and observed under the light microscope demonstrated epithelial stratification.

b) 4th passage ROE-2B cells processed for ultrastructural examination demonstrated desmosomes, tonofilaments and microvilli-like processes. Other intracytoplasmic organelles such as mitochondria, Golgi apparatus, and features suggestive of autophagosomes were also present.

c) Preconfluent ROE-2B cells stained with rhodanile blue, stained positive red for keratin.

d) Indirect immunoperoxidase staining was positive for CAM 5.2, thereby confirming expression of cytokeratin (characteristic of simple/glandular epithelium).

**Conclusion**

This study was the first reported odontogenic epithelial cell line. Both the technique applied and the cell line are promising tools for future biologic studies on molecular biology of normal odontogenic epithelium and epithelial odontogenic tumours, e.g. Ameloblastoma.

**C. QUANTITATIVE AGNORS AS DISCRIMINATOR BETWEEN BENIGN AND MALIGNANT ECTODERMAL ODONTOGENIC TUMOURS**

In this study, agyrophilic nucleolar organizer regions (AgNOR) was quantitatively stained for, to establish whether differences occur between Benign Epithelial Odontogenic Tumours without clear cell differentiation and Benign Epithelial Odontogenic Tumours with clear cell differentiation. Furthermore, the study also examined whether there is a quantitative AgNOR difference between Malignant Epithelial Odontogenic Tumours without clear cell differentiation and Malignant Epithelial Odontogenic Tumour with clear cell differentiation. This study became necessary in view of the opinion of Waldron et al 1985, that Ameloblastoma with clear cell differentiation should be treated as a low grade malignant neoplasm. However, Odukoya and Arole, 1992 reported a case of Clear Cell Ameloblastoma, which behaved clinically like a conventional ameloblastoma, was treated only by surgery, and did not recur 5 years after the surgery.

The number of nucleolar organizer regions (NOR) in each cell nucleus reflects cellular activity. The AgNOR method has been...
used in the scientific literature to discriminate between benign and malignant tumours.

The main finding from our study is that Benign Odontogenic Tumours with clear cell differentiation has a higher mean AgNOR score (360.6± 128.128) than its Benign counterpart that had no clear cell differentiation (263.2± 61.65). The difference was not statistically significant (p > 0.05). However, Malignant Epithelial Odontogenic Tumours with clear cell differentiation had a statistically significant higher mean AgNOR score (768.8± 211.7) than the malignant counterpart without clear cell differentiation (362.4± 80.94) (p < 0.05).

Conclusion
The study demonstrated that nuclear activity in epithelial odontogenic tumours significantly increased in malignant odontogenic epithelial tumours with clear cell differentiation. Therefore, clear cell differentiation may alter the biologic behaviour of epithelial odontogenic tumour.

4. THE DENTIST AND HOSPITAL MANAGEMENT

A. HOW THE DENTIST BECAME THE CHIEF MEDICAL DIRECTOR OF LAGOS UNIVERSITY TEACHING HOSPITAL

In December 1987, while serving as the Acting College Dean, School of Dental Sciences of the College of Medicine, University of Lagos, Professor Debo Adeyemi, who was then the Chief Medical Director of Lagos University Teaching Hospital, invited me for discussion on how I could assist LUTH to improve its Laboratory services. He stated further during the discussion that he had a plan to create a new administrative position of Coordinator of Laboratory Services, which will complement the effort of the Chairman, Medical Advisory Committee (CMAC) of LUTH, in achieving effective clinical services. I was enthusiastic to offer my services as requested, but worried about the logistic of serving two masters: the Vice Chancellor/Provost, being an Acting College Dean, and the Chief Medical Director, if appointed Coordinator of Laboratory Services. With the assurance from the Chief Medical Director that the LUTH part of the job would be facilitated for me, and the realization of the fact that my third term of the yearly renewable tenure as Acting College Dean would expire by 31st July 1998, I assured Professor Adeyemi that I would be willing to serve when officially appointed.

I was appointed Coordinator of Laboratory Services with effect from April, 1998. Although it was tedious combining this position with that of the Acting College Dean, I was able to cope through the grace of God. In the last week of July, 1998, while still serving both LUTH and CMUL, Professor Debo Adeyemi informed me that I would be assuming office as the Acting CMAC, LUTH, with effect from August 1998, when the term in office of Professor (Mrs) Odutola, who was then the CMAC, would have expired.

In order to strengthen the clinical services of the hospital, Dr. F.A. Durosinmi-Etti (who was then an Associate Professor, but later became a Professor), was appointed Coordinator of Clinical Services. Meanwhile, I combined the duties of Acting CMAC with that of Coordinator of Laboratory Services. I recall vividly that there was harmonious and cordial relationship between the Chief Medical Director, the Ag. CMAC, and the Coordinator of the Clinical Services.

A new dimension came into the story when I travelled (with the permission of the Chief Medical Director) to Cape Town in South Africa in the second half of August 1998, to present a paper at the International Association of Oral Pathology conference. Before I travelled, I had recommended that the Coordinator of Clinical Services should look after the office of the CMAC while I was away. During the ten days I was away, the Chief Medical Director, Professor Debo Adeyemi was appointed Honourable
Minister of Health, and had to appoint Professor Durosinmi-Etti, as Ag. Chief Medical Director and Ag. CMAC in order to avoid a vacuum, since I was away. This was the situation I met on ground when I returned from my trip to South Africa. The circumstances further dictated that I had to revert to the position of the Coordinator of Laboratory Services. Although unpalatable, I took the whole situation in good faith, with the satisfaction that I was rendering services to my nation, Nigeria. I recall with pride that during the period, the relationship that existed among the Honourable Minister of Health, the Ag. CMD/CMAC and my humble self was quite cordial. Administration of the Hospital also ran smoothly.

A further new dimension came into the story when it was time for regularization of appointment of the CMD and the CMAC by the Federal Ministry of Health. At the conclusion of the exercise, I was appointed the Ag. CMD/CMAC with effect from 1st November, 1998, while Professor Durosinmi-Etti reverted to his initial position as the Coordinator of Clinical Services. Both of us cooperated with each other in our new positions. The good relationship that existed then, remained so, even when Professor Durosinmi-Etti was later appointed Chief Medical Director of the National Hospital, Abuja. It is with gratitude to Almighty God that I remark that the brotherly and friendly relationship that had existed between Professor Durosinmi-Etti and I remains so till now.

It is remarkable that I served as the Ag. Chief Medical Director of LUTH from November 1998 to October 2000, when Dr. Tim Menakaya recommended me and the President of the Federal Republic of Nigeria, Chief Olusegun Obasanjo confirmed my appointment as Chief Medical Director of LUTH with effect from 1st November, 1998 for a period of 4 years.

When my first term tenure as Chief Medical Director expired in October, 2002, the Honourable Minister of Health, Professor A.B.C. Nwosu recommended renewal of my tenure to Mr. President of the Federal Republic of Nigeria, following recommendation of the Lagos University Teaching Hospital Management Board. Mr. President of the Federal Republic of Nigeria approved for me a second term of 4 years with effect from 1st November, 2002.

To the glory of the Almighty God, I became the first dentist in the history of the Lagos University Teaching Hospital to be appointed the Chief Medical Director of the Hospital. Furthermore, I became the first Chief Medical Director of LUTH to serve two terms in office.

B. THE EIGHT YEARS JOURNEY AS THE CHIEF MEDICAL DIRECTOR OF LUTH

The situation of the hospital in November 1998, when I assumed duty as the CMD of LUTH, dictated that there was need to focus on improved services in the hospital expeditiously. All efforts were therefore geared towards this objective. Most of the capital subventions received was used to procure equipment for improved patient care. The hospital benefited from critical care capital subventions which were judiciously utilized.

The hospital administration, under my leadership, demonstrated ability for expeditious emergency care responsiveness by successfully handling the epidemic of kerosene explosion burn victims in October 2001, and the Idiaraba crisis of February 2002, when many of the residents of Idiaraba community migrated in their hundreds to the Lagos University Teaching Hospital premises to take refuge, following the communal clash in the locality. The security of the refugees was guaranteed. Our job was facilitated when the Lagos State Government and a number of other non governmental organizations joined hand with LUTH Management to make the refugees comfortable, until the crisis was over.

The hospital administration, under my leadership, introduced, for the first time in LUTH, the Friend of the Needy Fund in year 2002, to cater for the hospital bills of truly indigent patients, who
hitherto, were detained in the wards until bailed out by good Samaritans. For the first time in the history of LUTH, all roads in the LUTH and College premises were named.

Although workers were often restive due to delay in payment of salaries and sometimes due to non implementation of government circulars, WORKERS FORUM was introduced in year 2000, as a conducive atmosphere for both management and workers to exchange views and be educated on how best to resolve any crisis that was in existence and proffer solution as to how such crisis could be averted in future. The WORKERS FORUM was found to be very effective.

Under my leadership, LUTH Administration put extra effort to ensure that adequate personnel emolument subventions were received in good time.

My second term tenure witnessed improved capital subventions and relatively more stable personnel subvention. Out of 53 developmental projects that were planned to be carried out, 47 were completely executed, while the remaining projects were at various stages of completion by the time I left office. Details of the projects can be found in my eight years tenure report, which has been submitted to the Federal Ministry of Health. Some copies are available in LUTH Administration.

My story on project development will be incomplete if I do not mention the VAMED Project. The Federal Government of Nigeria/ VAMED Engineering Project on equipment modernization of Teaching and Specialist Hospitals, valued to cost ₦1.08 billion, will go a long way to improve health care service delivery to patients by LUTH. I recall that the first batch of beneficiaries of the project were six Teaching Hospitals, each one located in each of the six geopolitical zones in the country. At the initial concept, University College Hospital in Ibadan was favoured to be the beneficiary of the slot for south west geopolitical zone. I recall that the LUTH Administration under my leadership lobbied the then Honourable Minister of Health, Dr. Tim Menakaya to consider LUTH among the beneficiaries in the first batch. With special thanks to the Almighty God, Dr. Tim Menakaya succeeded in convincing the Presidency to include LUTH as a beneficiary in the first batch. I should like to seize this opportunity to thank Dr. Tim Menakaya for the role he played in making us realize our dream for LUTH. I am happy to recall that before I left office, equipment list for LUTH had been concluded and order for purchase had been made. Furthermore some consignment of the equipment had started arriving on LUTH premises before I left office in October, 2006. Among services expected to improve significantly in LUTH as a result of the equipment modernization exercise are: operating theatre, radiotherapy, radiodiagnosis, mortuary, dental and physiotherapy services.

It is with gratitude to God and Mr. President of the Federal Republic of Nigeria, that I recall that shortfall in salary subvention was less experienced during my second term tenure as Chief Medical Director. For this reason, prompt and adequate payment of salaries were the order of the day, especially in the last one year of my stay in office.

I recall with satisfaction that LUTH Administration, under my leadership embarked on an aggressive fund generation drive that made it possible for quite a number of its overhead expenditure to be funded from the internally generated revenue.

LUTH Administration under my leadership also explored avenues for public private sector participation. Agreement was signed between LUTH Hospital Management Board and Messrs. First Foundation, whereby Messrs. First Foundation would bring in and operate Magnetic Resonance Imaging (MRI) radiological services in LUTH, and LUTH would share in the profit made by the company as well as own the equipment after Messrs. First Foundation has recovered the cost of MRI machine.
As part of the special attention paid to the public/private sector participation, three banks operated in the LUTH premises, and all have helped both in revenue collection as well as rendering philanthropic services to LUTH.

In an attempt to further improve revenue generation, LUTH Administration under my leadership advised the LUTH Management Board to set up LUTH Ventures, whose functions will include, among others, management of LUTH Intramural Private Practice.

Furthermore, Lagos University Teaching Hospital was the heartbeat of the nation as far as health care delivery is concerned. LUTH workers seem to be very much aware of this fact and therefore used to be the first to precipitate any crisis in the health sector, with the hope that Government's attention will be promptly received.

Therefore it should not surprise anyone that there were frequent industrial actions in LUTH, both during my tenure and those of my predecessors, despite series of dialogue with workers, in an attempt to abort such crisis.

C. THE CHALLENGES FACED BY THE DENTIST IN MANAGING A BIG TEACHING HOSPITAL SUCH AS LUTH

The first major challenge, especially at the initial stage, was that of acceptability by some colleagues. Even though the dentist shares the leadership of the health care delivery team with the medical colleague, quite a number of medical colleagues find it uneasy to readily accept the leadership of dentist. This probably explains why a classmate of mine, who happened to have read medicine asked me jokingly, what I was doing on the 'big seat' when he paid me an unscheduled visit during my early days in office. On my own part I did not feel deficient in any way because most of my friends and close associates read medicine. Furthermore in the course of my clinical practice and research activities I had worked closely with medical colleagues. I wish to use this opportunity to thank my close friends and especially some senior colleagues such as late Dr. Beko Ransome Kuti and Dr. Ore Falomo who were enthusiastic about my appointment and openly demonstrated support for me.

Another big challenge I faced was human management. Lagos University Teaching Hospital appears to be the melting point of all cultures in Nigeria. Therefore I had to put up a posture that was acceptable to these various cultures.

Also seen as an important challenge is the Nigerian factor in addressing issues of indiscipline by workers. The culprit is often connected to one influential person or the other. When it is time to administer disciplinary action, the Chief Executive sometimes
finds himself under pressure not to carry out the action so as not to displease some of the big wigs who may be interested in the culprit. So, we seem to pay lip service to enforcing discipline but the truth is that indiscipline thrives in our society.

With my eight years experience in office as CMD, I am convinced that many of the theories of management taught in the classroom do not work in managing LUTH. In fact, the more you apply some of these theories, the more you get into trouble.

D. MY EXIT FROM THE OFFICE OF THE CHIEF MEDICAL DIRECTOR

The various challenges enumerated above require an unusual administrative and management skill to survive more than one term as the Chief Medical Director of LUTH. Through consistent prayers and determination to succeed, to the Glory of God, I survived two terms.

I believe I will not be fair to the public and myself, and that I would not be doing enough justice to this section, if I do not make a few comments about my last three months in office. It was during this period that the Honourable Minister of Health, Professor Eyitayo Lambo, announced during a press conference that I should proceed on my terminal leave and that an interim Administrator was to assume duty with immediate effect. The letter that subsequently conveyed the directive further informed me that the Honourable Minister had received the report of the panel set up to investigate the circumstances that led to baby Eniola getting infected with the Human Immunodeficiency Virus, and that the White Paper on the report had been received.

Firstly, I wish to seize this opportunity to pray that God Almighty that gives good health shall shower His blessings upon this child and that the desire of her parents, like all parents do, that the child should grow up and become great in life, shall be granted. Amen. Secondly I wish to express my sincere appreciation to my friends, associates and well wishers, both from Nigeria and abroad, whose verdict was that of solidarity with me, rather than condemnation, with assurance that there was no way I should have been personally implicated in circumstances that led to the infection of the child. On my own part, I have neither seen any report so far that implicated me nor any report where LUTH accepted blame for the circumstances of the child. However, I am pleased with the report I have heard that the Federal Government will facilitate, through LUTH, establishment of an Endowment Fund for the child, and furthermore that all the support for successful rehabilitation of the child, which LUTH had been giving to the child from the time I was in office shall continue.

Finally I wish to thank the Honourable Minister of Health for ensuring that I finished technically, my two term tenure as Chief Medical Director of LUTH, which expired on 11th October, 2006.
5. RECOMMENDATIONS

a) Dental education in this country requires some upgrading. Operation of dental curriculum is capital intensive. If dental education has to be upgraded, Government must be prepared to put in a lot of capital funds. All dental operating units must function and dental consumables must be adequate.

My observation is that the present capacity for intake of dental students should not exceed 25 in a class. Any intake more than this will certainly overstretch the already inadequate facility.

I commend some of my colleagues who have excellent attitude to training of our students. Many colleagues need to refocus and readapt their attitude to favour satisfactory training of our students.

The presently operated dental curriculum which does not make provision for professional examination for dental students in Medicine and Surgery, need to be modified. In my undergraduate days, our set took professional examination in these two subjects and both lecturers and students took the subjects seriously. The background I had, has been beneficial to me. It has not only helped me in my clinical and research work, it also gave me confidence to perform, when I found myself heading a tertiary health institution.

Health Management and Entrepreneurship should be considered as a compulsory subject for all dental students to prepare them for leadership role in the health sector, and also expose them to opportunities available in the business world for successful business partnership between the health sector and other sectors.

b) Research activities in our dental schools require to be upgraded if we must keep up with the level of research that we see when we go for international conferences. This observation is based on my interactions with colleagues, dissertations received at Fellowship examinations of the postgraduate medical colleges of West Africa and Nigeria, and opportunity of serving as deputy editor of the *African Dental Journal* for several years. It could be argued that we need to customize our research to suit our community and environment. I share this belief as well, but in doing so we must be conscious of the fact that we need to move along with the changing world of research. For example, in the field of experimental oral carcinogenesis, the hamster buccal pouch model has been found very convenient, as carcinomas develop between 7 to 10 weeks of treatment with a carcinogen. All attempt to raise the hamster in our animal laboratory over the years was frustrating. We had to result to the rat model which takes nearly one year to develop carcinomas. We can all guess how frustrating it could be to maintain rats for such a long time just for a single study.

c) I will like to see a stronger influence of the central administration of the University of Lagos on the Idiaraba campus. By this I mean monthly salaries should be received simultaneously on the same day, both at the main campus and Idiaraba campus. Nowadays, I see staff quarters of staff working in the main campus properly fenced with wire mesh fencing, while those of staff in the medical area are fenced by plants and flowers planted around their houses.

Whatever the inadequacies that make the Idiaraba administration less prosperous should be promptly addressed before morale of staff, which is definitely affected, becomes more obvious.

d) In view of the fact that I have had the rare privilege of being the Chief Executive Officer of LUTH for eight years, I am inclined to make some recommendation in this area as well.

Transparency and accountability should remain the main focus of every Chief Medical Director of our tertiary health institutions.
Politics and too much bureaucracy must be avoided if the institutions must function effectively.

The present investment by government in the health institution is encouraging but government should strive to improve on the funding of these institutions.

The present reform going on in the health sector is good in principle. I pray that it should yield the desired effect. However, I believe that an accelerated action in some areas of reform should be able to add value to the ongoing reform.

One of such areas is to divide the administration of the Federal Ministry of Health into the following 2 sections:

i) Administrative Services section to be headed by a Permanent Secretary.

ii) Clinical Services section which must be headed by a Surgeon General, who must be a medical doctor or a dental surgeon, and whose rank must be that of a permanent secretary.

An alternative proposal is to leave all administration of the core Ministry of Health in the hands of the Permanent Secretary while a National Health Commission is established that is headed by a Director General (who must be a medical doctor or a dentist), whose function shall be to coordinate all clinical services in the Federation.

Finally, the issue of administration of each tertiary hospital requires some comments.

In order to ensure a hitch free administration and less stress for the Government, private investors should be asked to take over management of the hospitals. The hospital management should be profit oriented, such that there shall be cost recovery for investment in equipment etc, and from the income should be able to pay all staff and take care of all other overhead expenditure. Government should however be a shareholder in the investment. I strongly believe this could be a solution to many of the problems experienced in the health sector.
6. ACKNOWLEDGEMENT

Firstly, let me glorify the Almighty God for nurturing me and guiding me through life so far, from my humble beginning as a young child living with my parents on Tokunbo Street, very close to Upper Campus Street on the Lagos Island, an environment noted for street fighting, unusual smoking habits, and the nerve centre of hoodlums known nowadays as area boys, to my present status as a Professor of Oral Pathology, an Internationally recognized Oral Pathologist, and an Immediate past Chief Medical Director of the Lagos University Teaching Hospital.

We are blessed with four children who are a great source of joy and happiness to the family. They are our praying partners. The first child is Miss Adetoun Oluwafemi Odukoya, a 600 level undergraduate dental student of the University of Lagos. Our second child is Miss Temitope Tolulope Odukoya, a 500 level undergraduate dental student of the University of Lagos. Our third child is Master Temitayo Akintomide Odukoya, a 300 level Metallurgical and Materials Engineering student of the University of Lagos. Our fourth and last born is Master Oluwatobiloba Temiloluwa Odukoya, a JSS 1 student at the International School of the University of Lagos.

I also recognize and acknowledge an indefatigable personality who financed, encouraged and motivated me with respect to my education from primary school to the university level, after the death of my father in 1961. At the time this feat was performed the personality was only a primary school teacher. I introduce, with basket full of appreciation, my elder sister, Mrs. Elizabeth Iyabo Martins.

I acknowledge and recognize my elder brother, Venerable Samuel Bayo Odukoya, who has consistently supported me with prayers. I also recognize the family of my late elder brother, Mr. Emmanuel Onatoye Odukoya.

I acknowledge the presence of my mother-in-law, Mrs. M. A. Omoniyi, who has encouraged my wife to remain a pillar of support to me.

I recognize all members of my extended family and in-laws present here today.

I will like to spend the remaining part of this section, appreciating individuals outside my family, who made significant contributions to my life in the course of rising from nobody to become a professor of the University of Lagos.

Secondly, I wish to acknowledge my late parents, Mr. Michael Onajobi Odukoya, my father, a native of Odonopa, Ijebu Imusin in Ogun State, who died in May, 1961, and my amiable mother, Mrs. Janet Adetoun Odukoya, a true lover of peace, a native of Awe in Oyo State, who died in January, 1968.

At this point I will like to recognize my nuclear family, starting with my wife, Mrs. Rosemarie Oluwatoyin Titilope Odukoya, a LUTH trained nurse, Fellow of the West African College of Nursing and Member of the Nigerian Institute of Management, presently working as Industrial Nursing Sister with Nestle Nigeria Plc. Toyin, my wife, a strong Christian by faith and practice, has been a strong pillar of support for me since I got married to her in 1980. She was there for me, especially during my post doctoral training at Harvard School of Dental Medicine in Boston, U.S.A. She was also there for me praying and fasting ceaselessly during the eight years I served as Chief Medical Director of LUTH. She remained steadfast in prayers when I used to travel out of Lagos at short notice, stay late at work, and face industrial crisis and threats by LUTH workers. I publicly declare that Toyin truly qualifies as my jewel of inestimable value. Today, 6th June, 2007 is our 27th wedding anniversary. We give glory to Almighty God for His mercy and protection over the years.

We are blessed with four children who are a great source of joy and happiness to the family. They are our praying partners. The first child is Miss Adetoun Oluwafemi Odukoya, a 600 level undergraduate dental student of the University of Lagos. Our second child is Miss Temitope Tolulope Odukoya, a 500 level undergraduate dental student of the University of Lagos. Our third child is Master Temitayo Akintomide Odukoya, a 300 level Metallurgical and Materials Engineering student of the University of Lagos. Our fourth and last born is Master Oluwatobiloba Temiloluwa Odukoya, a JSS 1 student at the International School of the University of Lagos.

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I recognize all members of my extended family and in-laws present here today.

I will like to spend the remaining part of this section, appreciating individuals outside my family, who made significant contributions to my life in the course of rising from nobody to become a professor of the University of Lagos.
I appreciate Mr. A. O. Agboola, my biology teacher at Igbobi College, Yaba, Lagos, who saw me in the vicinity of the school field, looking sad, after the West African School Certificate Examination result had been released sometime in 1968, and wondered what was the matter, in view of the fact that I had a Grade 1 result with 7 distinctions. I told him that I felt I should have done better by scoring A1 in all subjects, if not for the death of my mother in January that year. He gave a lot of soothing words and encouraged me to look towards the future for a brighter tomorrow. Mr. Agboola also contributed to my choice of career. When he noticed that I was not in his biology class in my Lower Six (HSC 1), he sent for me and asked where I was. I told him that I was in the mathematics class. He then encouraged me to come to his biology class so that I could work towards a career in medicine in the future. He had no difficulty in convincing me and I immediately joined his class. I seize this opportunity to thank all my teachers at Igbobi College, for their contribution to my development in life.

I wish to seize this opportunity once more to appreciate all my lecturers at the undergraduate dental school at the College of Medicine, University of Lagos. I appreciate the three leading professors in the dental school during my undergraduate days: Professor Elijah Henshaw (presently, the Obong of Calabar), Professor Kunle Akinosi and Late Professor James Ana. I remember and appreciate all other lecturers, particularly, Professor Sam Akpata, Professor Adenubi, Professor A.L. Nwoku, (who I have always admired as a great teacher, and who still remains till today my friend and confidant, Professor Frank Okoisor, and finally Professor Yemi Mosadomi, who made it possible for me to travel to America to do my postdoctoral training at the Harvard School of Dental Medicine. I hereby express my sincere appreciation to Professor Ade Elebute, who was then the Provost of the College of Medicine at the time when I got approval for sponsorship by the University of Lagos to study at the Harvard School of Dental Medicine. These distinguished professors gave me the solid foundation that has made me an outstanding scholar today.

The man who truly made me what I am today in the field of Oral Pathology, my real idol, and my mentor is Professor Gerald Shklar, Retired Professor of Oral Pathology and Chairman of the Department of Oral Medicine and Pathology of the Harvard School of Dental Medicine, Boston, Massachusetts, U.S.A. According to some of his remarks during my first six months as his postdoctoral student in Oral Pathology, he saw me as a postdoctoral student with great potential and promised to make me popular worldwide through research. He actually fulfilled this promise as I did 8 published works with landmark findings with him before I left U.S.A in April, 1984. He also taught me humility in leadership position and when greatness is achieved. Furthermore, he enthusiastically wrote all recommendations about me, including the one that fetched me my Chair in Oral Pathology.

In the rough path that eventually culminated in my being the first dentist to be appointed Chief Medical Director of the Lagos University Teaching Hospital, and the first Chief Medical Director of LUTH to serve two terms, I wish to seize this opportunity to acknowledge the following people for their positive contributions:

a) Professor Debo Adeyemi, my predecessor in office, who was courageous enough to recommend a dentist to be the Acting Chief Medical Director.

b) Professor Francis Abayomi Durosini-Etti, who acted as the CMD for a brief period before my appointment, and who worked and cooperated with me as Coordinator of Clinical Services until he was appointed CMD of National Hospital Abuja.

c) Professor Dele Arigbabu, who served as the Chairman, Medical Advisory Committee for two terms for a total period of 4 years, during my tenure as CMD.
d) Professor Wale Oke, who served as the Chairman, Medical Advisory Committee after Professor Arigbabu, until July 2006.

e) Dr. Tim Menakaya, The Honorable Minister of Health, who recommended me for confirmation of Appointment as CMD for the first term tenure, from November 1998 to October, 2002.

f) Professor A.B.C. Nwosu, the Honorable Minister of Health, who recommended me for renewal of appointment for the second term tenure, which ended in October, 2006.

g) Top Management staff and the entire staff of LUTH for making it possible for me to serve them for two terms of 8 years.

h) Finally, I wish to thank Dr. Tosin Ajayi, Managing Director/Chief Executive of First Foundation Medical Engineering Company Limited, for fulfilling his promise to me, during my second term in office, that he would make available to LUTH patients, a Magnetic Resonance Imaging (MRI) services, when it became imminent that LUTH’s share of Federal Government allocation of funds for the VAMED PROJECT on equipment modernization, could not accommodate MRI, in view of equipment list LUTH had already presented for purchase. Before I left office, Memorandum of Understanding (MOU) had been signed between LUTH Management Board and Messrs First Foundation. The MOU contained a provision that gave LUTH opportunity to share in the profit that Messrs First Foundation would make from operation of the MRI services on LUTH premise. Although the MRI equipment cost over ₦400 million at installation, LUTH did not have to put down a penny, besides making available a space for installation of the equipment. Furthermore, the MOU had provision for the equipment to revert to LUTH after 5 years of successful operation. As at March ending, 2007, the equipment had been installed and backed up with a generator and a dedicated borehole for water supply to the equipment. Dr. Tosin Ajayi and his company deserve a round of applause. I pray for successful implementation of the MOU.

7. CONCLUSION

One thing I have come to realize over the years is that for as much as one remains in the academics, one is a student. Therefore, a functional academician is always in school learning all the time. On this basis, I would like to say emphatically that my career as a student since I started primary school at Holy Cross Cathedral Primary School, Lagos in 1956 up to this day, has been quite exciting, although bumpy, but quite fulfilling. I have made my mark internationally in the field of Oral Pathology, and my research activities have earned me awards both by the International Biographical Centre, England and the American Biographical Institute of the United State of America. Furthermore I have had the unique opportunity of serving as a Professor of Oral Pathology in the highly rated University of Lagos from 1996 to date. Equally exciting to me is the rare opportunity I have had to serve as the first dentist to be appointed the Chief Medical Director of the highly rated LUTH, and also the first CMD to serve for two terms. I believe this is a path that destiny has charted for me. I am also privileged that today, when my marriage is 27 years old, I have my family intact, blessed with a loving and supporting wife and four children in equal proportions of females to males, all of them progressing in their education. I give GLORY to the ALMIGHTY GOD who has made all these things possible for me.

I want to seize this opportunity to thank the immediate Past Vice-Chancellor of the University of Lagos, Professor Oye Ibidapo-Obe for granting my request to have this inaugural lecture today, which is a special day in the life of my family. I congratulate the Vice-Chancellor, University of Lagos, Professor Tolu Odugbemi, on his recent well-deserved appointment. I seize this opportunity
to thank the Vice-Chancellor for ensuring that this inaugural lecture, the first he is chairing since his assumption of office, holds today.

Mr. Vice-Chancellor, Sir, members on the high table, distinguished guests, ladies and gentlemen, I hereby end this inaugural lecture with quotation from the following chorus of a song "Blessed assurance – Jesus is mine........," the words of which were written by Fanny Crosby in 1873:

'This is my story, this is my song,
Praising my Saviour all the day long;
This is my story, this is my song,
Praising my Saviour all the day long.'

With the kind permission of Mr. Vice-Chancellor, I will like to sing this chorus only.

Thank you all for your attention.

8. REFERENCES


