



**MINERALIZED TISSUES AND THE OROFACIAL
REGION: MORPHOLOGY, COMPOSITION AND
DISEASE**

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July 2003

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Dallas, Texas, USA
PROFESSOR DR T. SOLHEIM
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DECLARATION

I, the undersigned, declare that the work contained in this presentation of publications is my own original work, as set forth in the statements which precede the published articles, and has not previously in its entirety or in part been submitted to any University for a degree.

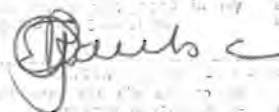

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E J RAUBENHEIMER

I certify that on the 7th day of Nov
declaration in my presence.


.....
COMMISSIONER OF OATH

2003 Erich Johann Raubenheimer signed this

1. Do you understand the nature and contents of the declaration?	Answer: YES
2. Do you intend to take the oath?	Answer: NO
3. Do you consider the signatory to be taking an oath?	Answer: YES


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Aaldert Pieter David

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DEDICATION

To my wife Claudia and our children for sustained encouragement, love and support

INTRODUCTION

My interest in research was initially stimulated by Prof J C G Slabbert, the then Head of Prosthodontics at the University of Pretoria, who supervised a study for which a fellow undergraduate student and myself won the Middleton Shaw award for undergraduate research at the annual meeting of the South African Division of the International Association for Dental Research. Upon completion of my undergraduate studies, Prof L M Jonck offered me a research position in the Department of Oral Pathology at the University of Pretoria, in anticipation of my then fiancée, and later wife, Claudia Noffke, to complete her studies in Dentistry. During that year I was exposed to both the practice of Dentistry on a part time basis and academic Dentistry, and I had no difficulty in deciding that my future would be in the latter. My decision to specialize in Oral Pathology was based on an observation that no other discipline in Dentistry serves as a more appropriate basis for research, a step that I have never regretted. Profs I W Simson and L Dreyer of the Department of Anatomical Pathology provided me with an exceptional training program in Histopathology, an aspect that I appreciate daily in my research and service-rendering program. Although specialization in Oral Pathology is academically more demanding than any other post graduate program in Dentistry, the first two Oral Pathologists to qualify from the University of Pretoria, Dr J Prinsloo and Dr A J Ligthelm (now Professor and Dean of the School of Dentistry at the same University) served as role models and proof that it was indeed possible to master the course.

Over the past 20 years in a diagnostic histopathologic service rendering capacity at a tertiary health center I have found myself at the rock face of a rapidly changing

discipline. Developments that revolutionized diagnostic histopathology, which was in the earlier years based on morphology, histochemistry and ultra structure only, have, although advancing accuracy, compounded the practice of the specialty. These developments include amongst others immunohistochemistry, histomorphometry and molecular pathology. Fruitful research cooperation with a more recently qualified colleague, Prof WFP Van Heerden, made my transition to molecular techniques easier. A fair representation of these techniques as well as many papers co-authored by Prof van Heerden are included in the list of publications submitted.

The morphology of normal tissues in and around the oral cavity is influenced by a multitude of local and systemic disease states. Through my diagnostic histopathologic service-rendering program that is focused on the orofacial region, a thorough understanding of the morphology of normal tissue types as well as localized- and systemic diseases afflicting this complex anatomical region has developed. The hardest tissue type and most difficult to prepare from an analytical point of view, namely teeth, are found in this region. Unlike most other laboratories dealing with microscopic techniques, those serving Oral Pathology departments are generally well acquainted with the preparation of mineralized tissue samples for analytical purposes. I am furthermore fortunate (from a researchers point of view) to be involved in the diagnosis of advanced pathology that is the result of patient ignorance and neglect, rendering our material the envy of many Oral Pathologists internationally. My wife, who qualified as a Dentomaxillofacial Radiologist joined our institution, and her enthusiasm for her subject resulted in several collaborative studies encompassing histopathology and radiology.

Many of the studies on large mammals were facilitated by South Africa's wealth in animals as well as the positive predisposition of the managers of our national parks towards research. The support services provided by the small staff component of the Department as well as the level of equipment in our laboratory are noteworthy. These positive factors in my working environment provided an opportunity to focus research programs on studies of normal and diseased mineralized- and soft tissues in man and animal.

The papers are grouped into four sections. Section 1 deals with multiple myeloma, its characteristic oral manifestations and complications. Section 2 encompasses several studies on mineralized tissues, teeth and bone. It includes histomorphometric studies on metabolic bone diseases as well as several projects that focus on human teeth and elephant ivory. Section 3 reflects studies on the normal structure- and neoplastic proliferations involving salivary glands. The role of the controversial myoepithelial cell in health and disease is highlighted and several diagnostic principles added to the study of salivary neoplasia. Section 4 is on diagnostic interpretation of jaw tumors and cysts. Contributions are made to the histopathologic and radiological interpretation of cysts and tumors of the jaws and in particular the late manifestations thereof.

ACKNOWLEDGEMENTS

1. My parents for their love and support and investing their hard earned money in my education.
2. My wife, Claudia for the sacrifices she has made to her career in order to facilitate my academic progress.
3. My children, Simon, Johann, Annika and Daniel for providing me with a reason to give my best.
4. My Secretary, Mrs. C S Begemann for typing and editing every manuscript generated during my career.
5. The laboratory staff of the Department of Oral Pathology at Medunsa and in particular Mr. J Hangelbroek, Mrs. Vorster and Mrs. E Mathibe for providing me with technological support.
6. The research management at Medunsa for their role in facilitating the funding of most of my research projects.
7. Prof. Willie van Heerden, a colleague and friend with whom I have co-authored many scientific papers.
8. The late Prof. J Dauth for introducing me to the art of preparing a scientific manuscript.
9. Mr. M J Dreyer of the Department of Chemical Pathology at Medunsa for his unselfish contributions to the biochemical analyses presented in this document.

10. The management of the National Parks Board for allowing our research team to harvest tissue during the culling program in the Kruger Park.

SUMMARY

This presentation consists of 50 selected publications that appeared in national and international peer reviewed journals over the past 19 years (1984 – 2003). The presentations are summarized under the following headings: Studies on multiple myeloma; Studies on mineralized tissues: Bone and teeth; Salivary glands: Normal structure and neoplastic proliferations and Diagnostic interpretation of jaw tumors and cysts.

Studies on multiple myeloma

In this section 7 publications are presented. The publications reported on the solitary tumorous orofacial presentation of multiple myeloma, ultrastructural appearance of neoplastic plasma cells as well as myeloma- associated amyloidogenesis with particular reference to deposits in the tongue. A theory on the cytogenesis of the distended endoplasmic reticulum in a case of non-secretory myeloma is presented. A unique study on salivary immunoglobulin concentrations in myeloma patients concludes this section.

Studies on mineralized tissues: Bone and teeth

Fourteen publications are presented in this section, four of which deal with static and dynamic histomorphometric studies on metabolic diseases of bone. The four publications include a review article on the histopathologic changes in metabolic bone disease states. In a series of cases of rickets a sub classification with therapeutic implications was proposed. Three publications reported on aspects of biochemical analyses of human

dentin. In the first study two new amino acids were discovered in dentin. The other two publications recorded the inorganic composition of opaque and translucent dentin and inorganic composition of tubular and inter tubular areas in dentin respectively. The last seven publications of this section deal with elephant ivory. Geographic variations in the composition ivory were established as well as a theory on the histogenesis of the unique chequered pattern thereof presented. Two manuscripts recorded the early development of the tush (or deciduous tusk) and tusk as well as tusklessness, and a theory on the latter phenomenon is presented. The morphology of the tush was established and one publication highlighted the importance of tusklessness as an indicator for the effect of ivory harvesting on the ivory bearing genome. The last publication demonstrated the value of trace elements in sourcing the origin of ivory.

Salivary glands: Normal structure and neoplastic proliferations

In this section, ten publications are presented. Embryology, functions and proliferative aspects of myoepithelial cells were analyzed in an invited review and aspects thereof emphasized in a manuscript which focused on salivary gland myoepithelium. A paper is presented on the structure of the salivary gland and composition of the saliva of the elephant. In a scanning electron microscopic study, aspects of the distribution of myoepithelium in the elephant salivary glands were reported. The remaining six publications deal with diagnostic aspects of series and case studies of salivary gland neoplasms in humans.

Diagnostic interpretation of jaw tumors and cysts

Nineteen publications are presented in this section. The uniqueness of most publications lies in the population sample studied. Most series on jaw tumors and cysts recorded internationally are on population samples in the northern hemisphere. Except for two publications that reported on jaw pathology recorded in Germany, all manuscripts in this section deal with pathology in a black South African population sample. Most studies analyzed histopathologic and radiological features of jaw tumors and emphasized the late manifestations thereof. A rare syndrome involving the development of enamel, absence of teeth and tumorous fibrous proliferations in the jaw was described and a molecular study identified a viral infection in an odontogenic tumor.

OPSOMMING

Hierdie voorlegging bestaan uit 50 geselekteerde publikasies wat in nasionale en internasionale wetenskaplike joernale oor die afgelope 19 jaar (1984 – 2003) gepubliseer was. Die voorlegging word opgesom onder die volgende hoofde: Studies van veelvuldige mielomatose; Studies van gemeneraliseerde weefsels: Been en tande; Speekselkliere: Normale struktuur en neoplastiese proliferasies; Diagnostiese interpretasie van kakebeen tumore en siste.

Studies van veelvuldige mielomatose

Sewe publikasies word in hierdie seksie aangebied. Hierdie publikasies beskryf die solitêre orofasiale kliniese presentasie van mieloom, ultrastrukturele voorkoms van neoplastiese plasmassel en mieloom geassosieerde amiloidose met spesifieke verwysing na die tong. 'n Teorie oor die sitogenese van die uitgesette endoplasmiese retikulum in 'n geval van nie-sekretierende mieloom word ingesluit. 'n Unieke studie wat handel oor die speeksel immunoglobulien inhoud van mieloom pasiente sluit hierdie seksie af.

Studies van gemeneraliseerde weefsel: Been en tande

Veertien publikasies word in hierdie seksie aangebied waarvan vier oor statiese en dinamiese histomorfometriese analises van been handel. Hierdie vier publikasies sluit 'n oorsigsartikel oor die histologiese veranderinge van metaboliese been siektes in. In 'n reeks pasiente met ragitis word 'n histologiese subklassifikasie, wat terapeutiese waarde het, voorgestel. Drie publikasies handel oor aspekte van die biochemiese samestelling

van menslike dentien. In die eerste hiervan word twee nuwe aminosure vir die eerste keer in dentien aangetoon. Die ander twee publikasies handel oor analises van die anorganiese samestelling van opaak en deursigtige dentien asook die verskille in die anorganiese samestelling van tubulêre en intertubulêre dentien. Die laaste sewe publikasies in die seksie het betrekking op olifant ivoor. Geografiese variasies in die samestelling van ivoor asook 'n teorie oor die histogenese van die unieke patroon in olifant ivoor word bespreek in twee voorleggings. 'n Verdere twee artikels handel oor die vroeë ontwikkeling van die primêre en permanente ivoortand asook tandloosheid en 'n teorie oor laasgenoemde verskynsel word aangebied. Die morfologie van die primêre ivoortand word vasgestel en in een publikasie word bespiegel oor die invloed van ivoor jag op die genoom van die Afrika olifant. Die laaste artikel in hierdie seksie toon die waarde van spoorelementele analises in die bepaling van die oorsprong van ivoor van die Afrika olifant.

Speekselkliere: Normale struktuur en neoplastiese proliferasies

In hierdie seksie word tien publikasies aangebied. Die embriologie, funksies asook proliferatiewe aspekte van die mioepiteelsel word ondersoek in 'n genooide oorsigsartikel en verdere aspekte daarvan word beklemtoon in 'n artikel wat fokus op mioepiteelselle in speekselkliere. Die struktuur van die parotis speekselklier asook die samestelling van die speeksel van die olifant word aangebied. In 'n aftaselektronmikroskopiese studie word aspekte van die distribusie van mioepiteelselle in die speekselkliere van olifante bespreek. Die laaste ses publikasies in hierdie seksie handel oor diagnostiese aspekte van speekselklier tumore in mense.

Diagnostiese interpretasie van kakebeen tumore en siste

Negentien publikasies word aangebied in die seksie. Hierdie studies is uitsonderlik daarin dat almal, met die uitsondering van twee, gevorderde kaakpatologie in swart Suid-Afrikaanse pasiente rapporteer. Die meeste publikasies analiseer die histopatologiese en radiologiese kenmerke van kaaktumore en presenter die laat manifestasies daarvan. 'n Raar sindroom, wat die ontwikkeling van emalje, afwesigheid van tande en tumoreuse bindweefsel vergroeiings insluit word beskryf en 'n molekulere studie rapporteer 'n virus infeksie in 'n odontogene tumor.

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