UNIVERSITEIT VAN PRETORIA
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# PATHOLOGY OF THE HEAD AND NECK: A RETROSPECTIVE APPRAISAL

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Published work submitted to the University of Pretoria for the degree of

Doctor of Science in Odontology (Oral Pathology)

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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 at any University for a degree.

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**WFP VAN HEERDEN**

I certify that on the ..14.. day of ...July.... 2003, Willem Francois Petrus van Heerden signed this declaration in my presence.

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## DEDICATION

To Marlene, Cherese and Bernice

# INTRODUCTION

The author graduated as a dentist (BChD) from the University of Pretoria in 1981 where after he completed his two-year compulsory national military service as a dental officer with the rank of lieutenant. He was stationed at the Maphuta-L-Malatji hospital, a rural hospital in the vicinity of Phalaborwa in the Limpopo province. It was during this period that his interest in Oral Pathology was stimulated. He was exposed to a wide spectrum of tumours and conditions of the head and neck and was fortunate to assist in many surgical procedures. After an eighteen-month period in general private practice in London, UK, he was appointed as registrar in Oral Pathology at the University of Pretoria. This four-year specialization course had laid the foundation for his future academic career. His training in Anatomical Pathology was under the expert guidance of Profs Ian Simson and Leonora Dreyer who were responsible for installing a foundation and passion for histopathology. The author completed his Oral Pathology training under the auspices of Prof At Ligthelm, the then head of Department of Oral Pathology and Oral Biology. He was also fortunate to be exposed to the Oral Pathology training programme at the University of the Witwatersrand under the supervision of Prof Mario Altini. The author completed his MChD degree (*cum laude*) in 1988 and was appointed as specialist/senior lecturer in the Department of Oral Pathology at the Medical University of Southern Africa (Medunsa). He worked at Medunsa with Prof Erich Raubenheimer for 8 years where after he was appointed as head of the Department of Oral Pathology and Oral

Biology, at his Alma Mater, The University of Pretoria. He obtained his PhD degree in 1998.

Oral pathology is the speciality of dentistry and pathology that deals with the nature, identification, and management of diseases affecting the oral and maxillofacial regions. It is a science that investigates the causes, processes and effects of these diseases. The practice of oral pathology includes research, diagnosis of diseases using clinical, radiographic, microscopic, biochemical or other examinations, and management of patients. Oral pathology is one the six specialities officially recognised by the Health Professions Council of South Africa.

Diagnostic histopathology is based on morphological features of the tissues examined. These entail the categorization of cells in the tissue, their morphology as well as their growth pattern. Apart from the standard haematoxylin and eosin staining, the use of histochemical and immunohistochemical techniques are widely used and are still the cornerstones of the diagnostic histopathological process. The rapid advancement in science and technology, especially in the field of molecular techniques, has contributed significantly to our understanding of the disease processes. The use of non-isotopic *in situ* hybridisation (NISH) to detect the presence of possible infective agents, the availability of high resolution DNA flow cytometry for ploidy analyses as well as the numerous applications of the polymerase chain reaction (PCR) are all accessible

techniques that have been used. These developments are reflected in the research profile of the author.

Participation in multi-disciplinary research programmes involving national or international collaboration is an important evaluation criterion in the allocation of research grants. This and the complexity of advanced techniques are reflected in the well-established fact that most research papers nowadays have multiple authors. Joint authorship from one department is also commonplace when such a department has more than one research interest.

The author was fortunate to be associated with outstanding researchers throughout his career. The enthusiasm and guidance received from Prof Erich Raubenheimer have played a valuable role in developing and stimulating his research interest. Their close collaboration is reflected in the number of co-authored publications. Similar collaborations with world authorities in specific fields have also lead to the successful completion of multidisciplinary research projects. The roles of Prof Joerg Hemmer, head of the division of Tumour Biology at the University of Ulm, Germany, with regard to high-resolution flow cytometry and Prof Estrelita van Rensburg, head of the Department of Medical Virology, University of Stellenbosch, with regard to molecular and viral associated research, need to be mentioned.

The papers are grouped into three sections. The first section deals with several studies on squamous cell carcinoma of the head and neck. It includes studies on the clinical presentation of oral cancer, the role of viruses in the development of oral squamous cell carcinoma, the potential of DNA flow cytometry in the management of this disease and the role of certain tumour suppressor genes in the oral carcinogenesis process. Section 2 includes several studies on tooth composition as well as the presentation of selected tumours and cysts of the jaws. Section 3 consists of studies on saliva and salivary gland neoplasms.

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- My parents for their love, encouragement and support.
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- Professors Ian Simson and Leonora Dreyer for being role models in my formative years as an Oral Pathologist.
- Professor Erich Raubenheimer, a colleague and friend, who introduced me to all the aspects of research and with whom I had the privilege of working and co-authored numerous scientific papers.
- Professors Joerg Hemmer and Estrelita van Rensburg for their friendship and valuable contribution towards the development of my academic career.
- My promoter Professor At Ligthelm under whom I qualified as an Oral Pathologist, for his advice and guidance throughout my academic career as well as in the preparation of this presentation.
- All my colleagues throughout my academic career, especially the very competent laboratory staff that I worked with.

# SUMMARY

This presentation consists of 52 selected publications that have appeared in national and international peer reviewed journals over the last 14 years (1989 – 2003). The presentation consists of the following headings: Studies on squamous cell carcinoma of the head and neck; dental hard tissues, tumours and cysts of the jaws and saliva and salivary gland neoplasms.

**Squamous cell carcinoma of the head and neck**

Twenty-three publications are presented in this section. The clinical and histological diagnostic criteria of oral cancer and premalignant lesions, especially aimed at the general practitioner, are discussed. Studies on the role of the Epstein-Barr and human papillomavirus in the pathogenesis of various squamous cell carcinomas of the head and neck region and different patient groups are included. The importance of DNA ploidy in oral carcinoma obtained with high-resolution flow cytometry is described. Valuable information can be obtained with this technique even when using archival paraffin-embedded tissues. Molecular studies, including gene sequencing and protein expression of the p53 suppressor gene as well as the *FHIT* gene, a candidate suppressor gene, were reported. This includes the evaluation of novel antibodies used for Fhit protein expression in oral squamous cell carcinomas.

**Dental hard tissues and tumours and cysts of the jaws**

In this section, 19 publications are presented. Two publications described the inorganic composition of dentine. The suitability of the sealing ability of a tri-cure glass ionomer material as a retrograde root filling material is illustrated. A unique case of permanent tooth germ injury is reported. A unusual case of amelogenesis imperfecta with multiple impactions associated with tumourous fibrous proliferations is described while a case of papillomavirus infection in an ameloblastoma is documented. The remaining publications include newly described entities as well as exceptional presentations of jaw tumours and cysts. The majority of these publications documented tumours and cysts in a Black African population and described the features seen in neglected and late presentation of these tumours.

**Saliva and salivary gland neoplasms**

Ten publications are presented in this section that include a study of immunoglobulin concentrations in saliva of multiple myeloma patients as well as the role of salivary glands in vertebrates. The remaining publications describe several aspects of salivary gland neoplasms. These include epidemiological data, diagnostic criteria, the role of DNA flow cytometry and unusual case presentations.

# CONTENTS

# LIST OF PUBLISHED SUBMISSIONS

## SECTION 1: STUDIES ON SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK