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A retrospective histopathologic review of paediatric oral and maxillofacial cases presented in Johannesburg: 1987-2007.

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of

Master of Science in Dentistry

Johannesburg, 2010.

DECLARATION

I, Clinton Munsamy, declare that this research report is my own work. It is being submitted for the degree of Master of Science in Dentistry to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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.....day of .....,2010

ABSTRACT

The characterisation of oral and maxillofacial histopathology found in children has been reported from developed countries of the west and in some developing countries in Africa but as yet not from South Africa. A retrospective study was designed to evaluate the epidemiological features of paediatric oral and maxillofacial histopathology seen at the University of the Witwatersrand's Division of Oral Pathology from January 1987 to December 2007. A total of 1,258 children ≤ 16 years of age with histologically confirmed disease in the oral and/or maxillofacial region were recorded, with a male to female ratio of 1:1,05. A progressive increase in the frequency of oral and maxillofacial lesions was seen with increase in the age of the patient. Most lesions were concentrated in the 13-16 year age group (41,5%). Pathology involving the jaw bones formed the largest category of all oral and maxillofacial pathologies (40% of the total number of cases) and was predominated by odontogenic cysts and tumours (61,8%). Odontogenic tumours showed a significantly higher frequency in children over 12-years of age (P=0,006). A higher frequency of unicystic ameloblastoma than in the literature was noted. The remaining pathology, in decreasing order of frequency, involved the oral and perioral soft tissues (31,6%), the salivary glands (18%), oral mucosa (8,9%) and dental hard tissues (1,7%). Most lesions of soft tissue and salivary gland were reactive / inflammatory in nature and were outweighed by fibro-epithelial polyps and extravasation mucoceles respectively. Nearly two-thirds of the oral mucosal lesions were benign Human Papilloma Virus-induced lesions. Malignant neoplasms comprised 4,1% of the total number of cases with Burkitt's lymphoma emerging as the most common malignancy.

Although the smallest number of biopsy specimens was obtained from children younger than 5-years of age, the likelihood of a malignant diagnosis in the latter age group was substantially higher than in older children.

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DEFINITION OF TERMS

Paediatric population: Perhaps surprisingly, there has been considerable variation between texts and studies regarding the age range that defines the paediatric population. In this research report, the term paediatric refers to individuals up to the age of 16 years i.e. the age when crown formation of all teeth approaches completion.

Oral and maxillofacial pathology: Diseases that affect the hard and/or soft tissues of the mouth, face and jaw.

CHAPTER ONE

1.0 INTRODUCTION

Most studies on the frequency of oral disease in children have been clinical surveys with emphasis on particularly the presence of caries and periodontal disease. Of those paediatric studies which assessed the frequency of oral conditions other than caries and periodontal inflammation, the diagnoses were largely made following oral examination and where clinical diagnostic criteria were applied to mucosal or soft tissue alterations of the oral cavity.[1-6] Although some oral mucosal anomalies and diseases such as angular cheilitis, linea alba, aphthous ulceration, herpes labialis and geographic tongue may be diagnosed on clinical grounds alone, oral and maxillofacial pathology encompasses a wide spectrum of diseases involving soft tissues as well as bony components and where an incisional or diagnostic excisional biopsy is often mandatory for a definitive diagnosis. There are, however, relatively few retrospective reviews on paediatric oral and maxillofacial pathology that are based on the analysis of biopsy records. Studies from Europe,[7] Asia,[8,9] Africa,[10-13] North America, [14-16] and South America [17-20] reveal a variation in the frequency and type of oral lesions in children from country to country.

A study conducted at the Department of Oral Pathology in Sheffield in the United Kingdom recorded the largest number of biopsy specimens submitted for histopathological study in the category of dental hard tissue abnormalities.[7] This finding contrasts remarkably with a Tanzanian study where malignant tumours constituted the diagnostic category with the largest number of specimens and where Burkitt's lymphoma represented the most frequently diagnosed lesion.[21]

Similar results were obtained from studies in other east African countries, notably from Kenya [22] and to a lesser extent from Uganda [23] and Nigeria.[24] Yet another African survey of biopsied paediatric oral lesions, however, showed the majority to be benign fibro-osseous lesions.[11]

Although much has been written about the epidemiology of paediatric oral and maxillofacial pathology in various countries around the world, no study has been conducted in any region of South Africa to evaluate the spectrum of oral pathology in the paediatric population at a service specialised in oral histopathological diagnosis. Such data would provide valuable insight about potential population differences by comparing the results of such a study with data previously published in the literature.

This study was therefore carried out so that the frequency and types of pathologies encountered in the oral and maxillofacial region of paediatric patients in Johannesburg, South Africa are established. This was done by analysing the histopathology records of biopsies from children examined at the University of the Witwatersrand's Division of Oral Pathology over a 20-year period.

CHAPTER TWO

2.0 AIM AND OBJECTIVES

2.1 Aim:

The aim of this study is to establish the epidemiology of oral and maxillofacial histopathology in children from birth to 16 years.

2.2 Objectives:

(i) To determine the **frequency** of oral and maxillofacial pathology, as diagnosed on biopsy, in the paediatric age group from birth to 16 years.

(ii) To establish the **age and gender distribution** of paediatric oral and maxillofacial lesions.

(iii) To establish the common **anatomical locations** of paediatric oral and maxillofacial lesions.

(iv) To identify the **types and frequency rates** of paediatric oral and maxillofacial lesions as diagnosed on biopsy.

(v) To identify **differences** in **ages** in children affected by:

- Odontogenic tumours and non-odontogenic tumours of bone.
- Malignant neoplasms of the oral and maxillofacial region.

CHAPTER THREE

3.0 LITERATURE REVIEW

3.1 Frequency of paediatric oral and maxillofacial pathology in histopathology biopsy services

The frequency of paediatric cases of oral histopathological biopsies varies across the globe. In Europe's largest paediatric-based survey of oral and maxillofacial pathology specimens submitted for diagnosis, Jones & Franklin.[7] found that children account for only 8,2% of all oral biopsies. Das *et al.*[15] and Skinner *et al.*[16] reported slightly higher frequencies of 12,3% and 12,8% respectively in North America. In similar studies conducted by Chen *et al.*[8] and Sato *et al.*[9] rates of 6,0% and 9,1% were found in China and Japan respectively. From the Indian subcontinent and southeast Asia, rates of 16,3% and 15,1% were reported,[25,26] while an African report[13] states that children are responsible for 20,2% of orofacial tumours in the population. Other African studies, conducted in different parts of Nigeria, found frequencies of 16,8% and 16,2% of total biopsies to be of paediatric origin,[11,12] with the highest frequency of 28% being documented in Ile-Ife in the Osun state of southwestern Nigeria.[27] In the Middle East, cases of oral and maxillofacial pathology in the paediatric population range from 5,5 to 23,0% of the total oral and perioral biopsies.[28] The frequency rates reported from some economically developing countries like Brazil (6,6%)[17,20] and Libya (8,9%),[10] however, appear much lower compared with sub-Saharan African studies.[11,12,27] Overall, the literature reflects greater involvement of African children in tumours and allied lesions of the oral and perioral structures as compared to occidentals and other non-African children.

3.2 Types and frequency rates of paediatric oral and maxillofacial pathology diagnosed on biopsy

3.2.1 Reactive / inflammatory lesions of the oral and maxillofacial region

Extraosseous, non-neoplastic, non-odontogenic lesions usually form the most common group of oral and maxillofacial pathology in childhood and adolescence with the greatest number of lesions falling into the inflammatory / reactive category. Studies report this category to be in the range from 15,7% to 66,1% of the total biopsies examined.[8,15,16,18,20,29] The cases reviewed in the study by Lima *et al.*[17] showed the mucocele as the most common of all lesions. Yamasoba *et al.*[30] compiled a 3,3-year study on lower labial mucosa mucoceles and showed that out of 70 cases, 70% were in the birth to 20 age group. Likewise, in several other studies the mucocele emerged as the most frequent histologically diagnosed lesion in children.[8,15,18] Exceptions to this finding include the surveys conducted by Ulmansky *et al.*,[28] Gültelkin *et al.*,[29] Aregbesola *et al.*[27]and Elarbi *et al.*[10] where fibroma, peripheral giant cell granuloma, fibrous epulis, and pyogenic granuloma ranked as the most common lesions respectively.

Lima *et al.*[17] in their study reported an 8% frequency of non-specific mucositis in oral biopsies from children in Pelotas-Brazil between 1983 and 2002. The frequency of non-specific chronic ulceration ranged from 0,16% to 0,9% of the total biopsies in the surveys conducted by Dhanuthai *et al*.[25] and Jones *et al*.[7] respectively. Although far less common, immune mediated inflammatory lesions of the oral mucosa were also documented in surveys of biopsies from

children. These included the myriad of cell and humoral mediated autoimmune diseases, such as lichen planus, lichenoid reaction, graft versus host disease, benign mucous membrane pemphigoid, pemphigus vulgaris, discoid lupus erythematosus, erythema multiforme, psoriasis, sarcoidosis, orofacial granulomatosis, Crohn's disease and Behcet's syndrome.[7,18,31] Foreign body reactions were a frequent cause of granulomatous inflammation in a study conducted in the United Kingdom while mycobacterial infection was less frequent and deep fungal infection never mentioned.[7]

Periapical granulomas also ranked high in the inflammatory category in most cited surveys.[7,15,17,18,25] Lima *et al.*[17] reported a 5,28% occurrence rate in patients up to the age of 14 years while Jones *et al.*[7] found the periapical granuloma represented the second most frequently diagnosed lesion constituting 7,5% of their total biopsy material from children. Sequestra / chronic suppurative osteomyelitis were rarely documented in most surveys of biopsy material obtained from children. The largest number of histologically confirmed cases (2,96%) has thus far been described among Thai children in a 15-year retrospective study of paediatric oral biopsies.[25] This is followed closely by the survey performed by Keszler *et al.* (2,2%) who studied the population of Argentina, a Latin-American country south of Brazil.[20]

3.2.2 Benign lesions of oral mucosa and soft tissue

Most reports indicate squamous papilloma as the most prevalent benign lesion of oral mucosa.[7,9,15-18,25,28,32] Al-Khateeb *et al.*[32] conducted a survey of 258 cases of children ranging in age from birth to 18 years and showed a 13,2% rate of occurrence for squamous papilloma.

These authors reported the most frequent locations as the tongue, lower lip and palate with a peak frequency in the 12-18 year age group. Jones *et al.*[7] conducted a 30-year study of children ranging in age from birth to 16 years and found a 4,2% rate of occurrence of squamous papillomas with an almost equal gender distribution. The low percentage (0,4%) of squamous papilloma in a study from southern Taiwan[8] and in a recent analysis of 213 Libyan children and adolescents [10] remains unexplained, but may be due to geographic variations.

Common benign soft tissue tumours included benign nerve sheath tumours, in particular neurofibromas; melanocytic nevi, lipomas and to a lesser extent congenital epulis, angiofibroma, angiomyoma and benign fibrous histiocytoma.[7,17,25] Sato *et al*.[9] and Al-Khateeb *et al.*[32] pointed out the tendency of the haemangioma as the most frequent paediatric diagnosis in the Japanese and Jordanian populations respectively. While controversies in the terminology and classification of haemangiomas prevail, these authors considered haemangiomas as hamartomatous lesions that are probably developmental in aetiology.[9,32]

3.2.3 Non-odontogenic cysts of soft tissue

Chen *et al.*[8] reported that 98% of the cystic lesions in their study were located in the jaw. Of the limited number of studies which documented the occurrence of non-odontogenic cysts in soft tissue, the epidermoid cyst was the most common.[7,8,15,18] This was followed in one study by the dermoid cyst and the oral lymphoepithelial cyst.[7] Most studies, however, considered only solid tumour and tumour-like lesions while cystic lesions of bone and soft tissue were entirely excluded.[9,10,13,27,28,32]

3.2.4 Salivary gland neoplasms

There are few large series regarding salivary gland tumours in children and adolescents in the English language literature.[33,34] Although salivary tumours are rare within paediatric populations, a 1:1 ratio of benign to malignant salivary tumours has generally been reported.[7,33] Most of these tumours occur in the second decade of life, with a mean of 14 years and with malignancies showing a mean age lower than that of patients with benign tumours.[33] As in adults, pleomorphic adenoma is the most common epithelial salivary gland neoplasm in children, the parotids are the most frequently involved site and there is a predilection for the female gender.[35] According to Fonseca *et al.*[36] malignant salivary neoplasms in young patients are most common in the intraoral minor salivary glands.

3.2.5 Cystic lesions of bone

The distribution of jaw cysts in the general population is as follows: radicular cysts 52,2%, dentigerous cysts 17,1%, nasopalatine duct cysts 11,6%, odontogenic keratocysts 10,2%, simple or traumatic bone cysts 1% and eruption cyst 0,8%.[37] Several studies that have examined the frequency rates of oral and maxillofacial pathologies encountered during childhood and adolescence have shown that the distribution of jaw cysts during this period differs from that found in the general population. Bodner[38] analysed 69 patients, mean age of 9,7 years, with cystic lesions of the jaw. In the latter study, dentigerous cysts were most common (44%), followed by eruption cysts (22%), traumatic bone cysts (17,7%), radicular cysts (13,3%) and odontogenic keratocysts (1,5%).[38]

In the study by Dhanuthai *et al.*[25] cystic lesions of bone represented the most common diagnostic category and comprised 35% of all paediatric oral lesions. The authors studied the population of Thailand and found the dentigerous cyst to be the most common paediatric oral lesion,[25] as was also found in a Brazilian study by Maia *et al.*[19] Shah *et al.*[14] also showed that dentigerous cysts were most common in their survey of oral biopsies in a paediatric population in San Francisco. Despite the geographic proximity, however, Das *et al.*[15]found that the mucoc5ele was overwhelmingly the most common lesion biopsied in children in Chicago. This observation reflects the differences in distribution of lesions between different areas despite having similar political and social conditions.

It has been reported in previous studies that dentigerous cysts, followed by radicular cysts are the most frequently encountered odontogenic cysts in paediatric populations.[8,17,18,19,25,29] Jones *et al.*[7] found the ratio of odontogenic to non-odontogenic cysts to be 7,8:1. Their survey also recorded the largest number of non-odontogenic cysts (n=67) in children where the solitary bone cyst was the most frequent non-odontogenic cyst (n=19), constituting 28,4% of the cases in the group of non-odontogenic cysts and which was closely followed by the nasopalatine duct cyst (n=17).[7] In Das and Das' report, out of 15 non-odontogenic cysts 10 were solitary bone cysts and 5 were aneurysmal bone cysts.[15]

3.2.6 Benign non-odontogenic tumours of bone

The view that paediatric jaw bone tumours are usually non-odontogenic does not apply to most contemporary studies since 61% to 78,4% of the jaw bone tumours in recent studies were odontogenic in origin.[7-10,17,18,25,32] From the total of 625 biopsies received in a 20-year period, from children up to the age of 14 years, benign jaw tumours consisted of 42 (77,8%) odontogenic tumours and 12 (22,2%) non-odontogenic tumours,[17] while in another study from a total of 1251 biopsies received in a 15-year period, from children up to the age of 16 years, benign jaw tumours consisted of 257 (78,4%) odontogenic tumours and 71 (21,6%) non-odontogenic tumours.[25]

In most studies the most common benign non-odontogenic tumour fell into the benign fibro-osseous lesion category,[10,13,18,25,27] with fibrous dysplasia being most frequent.[8,11,21,25,27] Cemento-ossifying fibroma (n=9), fibrous dysplasia (n=7) and cemento-osseous dysplasia (n=1), accounted for 15% of the benign non-odontogenic tumours of the jaw in a Nigerian paediatric series,[13] while in a subsequent study that was also conducted among Nigerian children; 68,6% of benign non-odontogenic tumours occurred as fibro-osseous lesions but exclusively as fibrous dysplasia (n=35).[11] From these results, it would appear that the benign fibro-osseous lesions do not show a consistent racial distribution in the paediatric population. A similar bearing comes forth for the central giant cell granuloma which showed similar frequencies of 0% to 1,4% and 0% to 3,2% in African[11,13] and Brazilian[17,18] paediatric populations respectively. The Brazilian studies[17,18] were both undertaken in the birth to 14 year age group and spanned an average time period of 17,5 years while both Nigerian studies[11,13] were undertaken in the birth to 15 year age group with the average time range of the study being 10 years.

3.2.7 Benign odontogenic tumours

Some researchers declare that odontogenic tumours are rare in children and account for <1% of the total biopsies seen in children up to the age of 16 years,[7] while others have shown frequency rates as high as 25,9% for the same age group.[11] Jones and Franklin,[7] in their analysis of 4406 oral and maxillofacial pathology specimens from children up to the age of 16 years found that 243 (5,5%) children had odontogenic tumours. Adebayo *et al.*[11] studied the incidence and frequency rates of childhood oral and perioral tumour and tumour-like lesions in Nigeria over a 20-year period. These authors found the frequency rate of odontogenic tumours (25,9%) was much higher than that reported in western countries.

The distribution of odontogenic tumours in children is also controversial. The World Health Organisation in 2005 published some major changes in the classification of benign and malignant odontogenic tumours, the striking feature being inclusion of odontogenic keratocyst as a benign tumour of odontogenic epithelium, termed as keratocystic odontogenic tumour.[39] Elarbi *et al.*,[10] found the second most common odontogenic tumour was the keratocystic odontogenic tumour at 20% of all odontogenic tumours. In the study by Lima *et al.*[17] 625 cases were studied and odontogenic tumours, which made up 6,72% of the total biopsies studied, were made up of only odontoma (n=27) and keratocystic odontogenic tumour (n=10). In all other papers on this subject, the odontogenic keratocyst has been catalogued as a developmental odontogenic cyst.

Most studies from sub-Saharan Africa report a higher frequency of ameloblastoma compared to other odontogenic tumours.[11-13,27] This finding differs from similar surveys that were conducted

in Europe,[7] North America,[15,16] South America,[17,18] Japan,[9] and Jordan, [32] which showed that the odontoma represented the most common odontogenic tumour in children. In the literature there are also occasional variant papers that report myxoma and adenomatoid odontogenic tumour as the most common paediatric odontogenic tumour.[28,40]

3.2.8 Malignant tumours

The frequency of primary malignant oral tumours in children varies in different parts of the world. Although most cases of oral neoplasms in children are benign, in some paediatric studies malignant oral neoplasms were more frequent than benign tumours.[40] This is due to the relative frequency of Burkitt's lymphoma in Africa. A study that was carried out in Tanzania, involving biopsy materials examined from 1982 to 1997, found Burkitt's lymphoma to be by far the most common oral malignant lesion accounting for 88,2% of all malignancies, followed by squamous cell carcinoma and Kaposi's sarcoma.[21] Contrary to most reports,[9,20,26,28,41] Aregbesola *et al.*[27] also found a high percentage (51%) of malignant tumours. These authors found that Burkitt's lymphoma accounted for 45% of all the tumours and 89% of the malignant tumours.[27] Even in those non-African studies which document a low frequency of oral malignancies in children, Burkitt's lymphoma emerges as the commonest malignant orofacial tumour of childhood.[10,25,28]

Rhabdomyosarcoma is considered the most common childhood malignant soft tissue tumour accounting for some 5% to 10% of all childhood malignancies.[42] In children, rhabdomyosarcoma has a relative predilection to the head and neck region, forming almost a third of malignant tumours in this location.[42] This tumour was also the most common malignant tumour seen in the

oral and maxillofacial region in various other studies.[7,17,32] Contrary to these surveys, however, is the finding of Kalyanyama *et al.*[21] who reported Kaposi sarcoma as the most common mesenchymal cancer in Tanzanian children. Furthermore, unlike the reports of Elarbi *et al.*,[10] Dhanuthai *et al.*,[25] Jones *et al.*,[7] Aregbesola *et al.*,[27] Al-Khateeb *et al.*,[32] that emanated from Libya, Thailand, United Kingdom, Nigeria and Jordan respectively, no osteogenic sarcomas were diagnosed in the Brazilian paediatric surveys by Lima *et al.* [17]and Sousa *et al.*,[18] in the Japanese paediatric surveys by Chen *et al.*[8] and Sato *et al.*[9] and in the American paediatric surveys by Das *et al.*[15] and Skinner *et al.*[16] This shows that the preponderance of some malignancies in certain countries and yet not in others is nearly universal and perhaps with racial peculiarities.

More than 30 years ago, it has been stated, that in children for every carcinoma there will be 6,3 sarcomas while in adults for every sarcoma there will be 7,5 cases of carcinoma.[43] The results of more recent analyses, however, show a relatively higher frequency of carcinomas in children than was previously thought,[44] with the sarcoma to carcinoma ratios varying from 3:1[10] to 2:1[25] to nearly 1:1.[7] The malignant epithelial tumours in children remain dominated by malignancies of salivary glands with mucoepidermoid carcinoma predominating.[33]

3.3 Age distribution of paediatric oral and maxillofacial pathology

In the paediatric population, the overall frequency of diagnosed specimens from the oral and maxillofacial region is highest in the mixed dentition period (> 6-12 years), with a mean age of 11 years, while children below 5 years are the least affected.[25,29] In the report by Dhanuthai *et*

al.,[25] out of 1251 cases, 616 (49,2%) were from children between the ages of 6 and 12 years. In a study by Gultelkin *et al.*,[29] 472 oral biopsies from patients up to 15 years of age were studied and 283 (60%) were in the 6 to 12-year age group.

Al-Khateeb *et al.*[32] found the mean age for children with oral and maxillofacial histopathology to be 11 years. Their study population was divided into 3 age groups: group 1 (≤ 5 years), group 2 (6-11 years) and group 3 (12-18 years). Hemangioma was the most common benign soft tissue tumour in all age groups. Among children less than 6-years old, there were only two benign jaw tumours, namely cementifying fibroma and central hemangioma. Malignant tumours in this age group were lymphoma (n=7) and rhabdomyosarcoma (n=6). In the age group 6–11 years, odontoma was the most common benign jaw tumour. Common malignant tumours in this age group included rhabdomyosarcoma and lymphoma. Among adolescents (12–18 years old), common benign jaw tumours were odontoma and central giant cell granuloma.

Sato *et al.*[9] in their study on oral and maxillofacial tumours in children found the largest number of lesions in the 6 to 11 year age group with the ages of the patients ranging from 4 months to 15 years. Twenty-four patients (9,6%) were less than 1-year old. In the group under 6 years of age, lymphangiomas and hemangiomas were most common and 20 angiomas (21% of all angiomas in their study) were seen in patients less than 1-year old. Twenty-five of the 27 ameloblastomas were diagnosed in patients over 12 years of age. Although crown formation is completed by 4- or 5-years of age in most of the permanent teeth, it is interesting to note that in all relevant studies there were significantly more odontogenic tumours in children over 6-years of age.[9,32] This finding militates against origin of odontogenic tumours from the developing tooth germ.

3.4 Gender distribution of paediatric oral and maxillofacial pathology

The overall male to female ratio for oral and maxillofacial biopsy specimens received from paediatric patients is in the region of 1,4:1.[7,11,13,27,32] Dhanuthai *et al.*[25] in their study, reported no statistical difference in the occurrence of oral and maxillofacial lesions between genders (M:F=1,05:1), except in the primary dentition period group (M:F=1,9:1). At variance with the findings of Dhanuthai *et al.*,[25] Aregbesola *et al.*[27] found there were more boys in all the age groups, except between 15 and 19 years when there was no difference. In most studies malignant tumours affected more males than females to varying degrees with male:female ratios of 1,6:1;[10] 2,7:1;[25] 2,5:1;[27] 2:1;[11] 3:2;[28] and 2,1:1.[13]

There is conflicting data with regard to the gender distribution of odontogenic tumours in children. Ulmansky *et al.*[28] reported that a larger number of benign odontogenic neoplasms were seen in Israeli girls than in boys, while the male:female ratio for odontogenic tumours in Nigeria was 1,6 to 1,[13] with an almost equal gender distribution found in Libyan children.[10] In the general population the sex predilection for ameloblastoma, the most common benign odontogenic tumour, is also equivocal in the literature. Many workers report a male preponderance[13,45-47] while a few [28,48] claim otherwise or found that both genders were equally affected.[49] A similar discordance is noted in paediatric studies on this subject. In a Japanese study, a slight female predominance was found in patients with ameloblastoma,[8] which correlates with the report of Kahn.[50] This is, however, in contrast to a study on Nigerian children by Arotiba,[13] who reported a male predominance and also in contrast to the study of Chidzonga,[51]

who found no differences in the occurrence of ameloblastoma between the sexes in paediatric patients. The gender predilection for myxoma, regardless of age, appears to favour females[46,52] with Keszler *et al.*[20] reporting a female-to-male ratio of 3:2 for Argentinian children and Adebayo *et al.*[11] reporting a female-to-male ratio of 2:1 for Nigerian children. The results of most studies indicate that there is a nearly equal distribution of odontomes among males and females,[53] while the study by Chen *et al.*[8] demonstrated a definite male predominance. From large-scale studies of all ages, it appears that most odontogenic cysts, including the odontogenic keratocyst (keratocystic odontogenic tumour) is more frequent in males than females.[54]

For the tumour-like fibrogranulomatous lesions (pyogenic granuloma, fibroepithelial polyp, epulis, peripheral cemento-ossifying fibroma), females usually outnumbered males.[10,25] In the work by Elarbi *et al.*[10] patients in the 10 to 14-year age group accounted for most of these lesions. They hypothesised that a high involvement of the female sex and more patients in age group of 10 to 14-years could possibly emphasise the role of hormones responsible for these kinds of lesions.

3.5 Anatomical locations of paediatric oral and maxillofacial pathology

Al-Khateeb *et al.*,[32] Sato *et al*[9] and Bhaskar[55] found that among the sites commonly involved by oral and maxillofacial tumours in children and adolescents were the lower lip and tongue. This finding corresponded with the location of the most common histological diagnosis of haemangioma in these studies. Lima *et al.*[17] in their study on oral and maxillofacial biopsies in

children found that the number of bone biopsies exceeded those of soft tissue with the maxillary bone being the most commonly affected site, followed by the mandible and the lower lip. This finding in turn corresponded with the combined higher frequency of dentigerous cysts, pericoronal follicles and periapical cysts when compared with soft tissue / mucosal pathology. Contrary to these findings Das *et al.*[15] reported the periodontium as the most commonly biopsied site, followed by lips and oral mucosa. Tongue, palate and floor of the mouth followed in descending order. The number of biopsies from the lower jaw was also much higher than from the upper jaw.

According to the above literature review, there exists considerable variation in the frequency, types, age, gender and site distributions of oral and maxillofacial histopathology from children and adolescents in various parts of the world. Since no such study has thus far been undertaken in South Africa, the need for a study of this nature to establish the aforementioned parameters in a South African population becomes apparent. This knowledge will allow for the determination of similarities and differences that exist between our observations and those of other workers in previous studies. It may also contribute to the effective planning of educational programs for dental students, primary care dentists and other specialists in the head and neck field.

CHAPTER FOUR

4.0 MATERIALS AND METHODS

4.1 Study population

Children with histologically confirmed pathology in the oral and/or maxillofacial region were studied.

4.1.1 Inclusion criteria

Children were included if they met the following criteria:

- Male or female children with an age of 16 years or younger with pathology that manifested in the oral and/or maxillofacial region.
- Children from whom biopsies from the oral and/or maxillofacial region were submitted for histological evaluation to the Division of Oral Pathology from January 1987 to December 2007.

4.1.2 Exclusion criteria

- Children above 16 years.
- Children with pathology involving only the neck lymph nodes.
- Children with dermatopathology in the perioral, facial or neck area.
- Children from whom biopsy material showed normal tissue.
- Those diagnoses that were inconclusive, either due to an inadequate biopsy specimen or insufficient clinical data.

- Fine needle aspirate biopsies.

4.2 Study setting

Biopsy records were retrieved over a 20-year period (January 1987 to December 2007) from the files of the Division of Oral Pathology at the University of the Witwatersrand in Johannesburg. This department provides a diagnostic service not only to the Charlotte-Maxeke Johannesburg Hospital but also to municipal community clinics and other provincial hospitals within Johannesburg and surrounding areas, in particular the Chris Hani-Baragwanath and the Helen Joseph Hospitals. This regional wide biopsy service started in June 1999 when several public health laboratory services were united. During this period the histopathology laboratory of the Division of Oral Pathology at the University of the Witwatersrand merged with the National Health Laboratory Service Johannesburg histopathology laboratory.

Chris Hani Baragwanath Hospital is the largest hospital in South Africa and one of the largest hospitals in the world, consisting of 429 buildings spread out over extensive grounds which occupy 173 acres (0,70 km^2). The hospital is in the Soweto (South-Western Township) area of Johannesburg, South Africa. It is the main health-care facility serving the residents of this vast African township and people in the surrounding areas who often do not have medical insurance facilities. It also serves as a referral hospital for smaller hospitals in Gauteng. This specialist hospital further has links to an academic teaching and research institution – i.e. the University of the Witwatersrand Health Sciences Faculty.

The Charlotte-Maxeke Johannesburg Hospital is the main teaching hospital for the University of the Witwatersrand, Faculty of Health Sciences. The hospital is also one of the four tertiary hospitals for Gauteng Province and serves both the poor and middle class people who may have medical insurance facilities. Since the Oral Pathology Division at the University of the Witwatersrand receives biopsy specimens from amongst the largest and major referral hospitals in Johannesburg and surrounding areas, the information obtained from this study is considered to be representative of the greater Johannesburg and surrounding areas' population.

4.3 Study design

A retrospective study design was used to study the epidemiology of oral and maxillofacial histopathology from January 1987 to December 2007. A review of patients' biopsy records enabled the author to establish the epidemiology of paediatric oral and maxillofacial histopathology among the study population. Data from a retrospective study is fairly representative and minimizes possibilities of bias compared to a cross-sectional study.

4.4 Data collection

A data capture sheet based on study objectives was developed and used (Appendix 1). Data obtained from this study included the subject's age, gender, anatomical location of the biopsied lesion and the final histological diagnosis.

4.5 Data analysis

Data was entered into Microsoft Excel. To facilitate organisation of the data and to provide a comprehensive review of the histopathological diagnoses encountered in the paediatric population diagnoses were compiled into the following diagnostic categories: bone pathology, soft tissue pathology, salivary gland pathology, mucosal pathology and pathology of the dental hard tissues.

The study population was divided into four age groups: group 1 (0-4 years), group 2 (5-8 years), group 3 (9-12 years) and group 4 (13-16 years). The purpose of dividing the subjects into these four age groups was to note the frequency of oral biopsied lesions relative to age. The study population was also divided into a mixed dentition group (≤12 years) and early permanent dentition group (>12 years) for analysis of the frequency of distribution of odontogenic pathology relative to the developmental stage of the dentition.

Descriptive statistics were first carried out for key variables (age, gender, site of biopsy). The incidences of the lesions were determined, and the absolute and relative frequencies were obtained and expressed as percentages. Means and standard deviations were used for continuous variables while proportions and graphs were used for categorical variables. Graphs were plotted using Microsoft Excel. Statistically significant differences in categorical variables were assessed using the Fisher's exact test. A *p*-value less than 0,05 indicated a statistically significant finding.

4.6 Ethical considerations

The protection of the rights of human research subjects was taken into consideration. Although this study was a retrospective study where there was no direct contact with the subjects, ethical clearance (M080850) was still obtained from the Human Research Ethics Committee at the University of the Witwatersrand (Appendix 2) and the subjects remained anonymous.

CHAPTER FIVE

5.0 RESULTS

5.1 Frequency of oral and maxillofacial pathology in the paediatric population

1367 biopsy specimens were found for children ≤ 16 years from January 1987 to December 2007. Of these, 109 (7,9%) were excluded because they did not meet the inclusion criteria. A total of 1258 biopsy cases were consequently included in this study. This represented 6,5% of the total number of biopsy specimens (19,369) received during this period at the Division of Oral Pathology of the University of the Witwatersrand.

5.2. Subjects' demographic characteristics

5.2.1 Age

The mean age of the study subjects was 10,7 years with a standard deviation of 4,01 years. The youngest patient was 1 month old while the oldest was 16 years.

An increase in the frequency of oral and maxillofacial histopathological diagnoses with increasing age was noted in this study and the majority 522 (41,5%) of cases were concentrated in the 13-16 year age group (Figure 1).

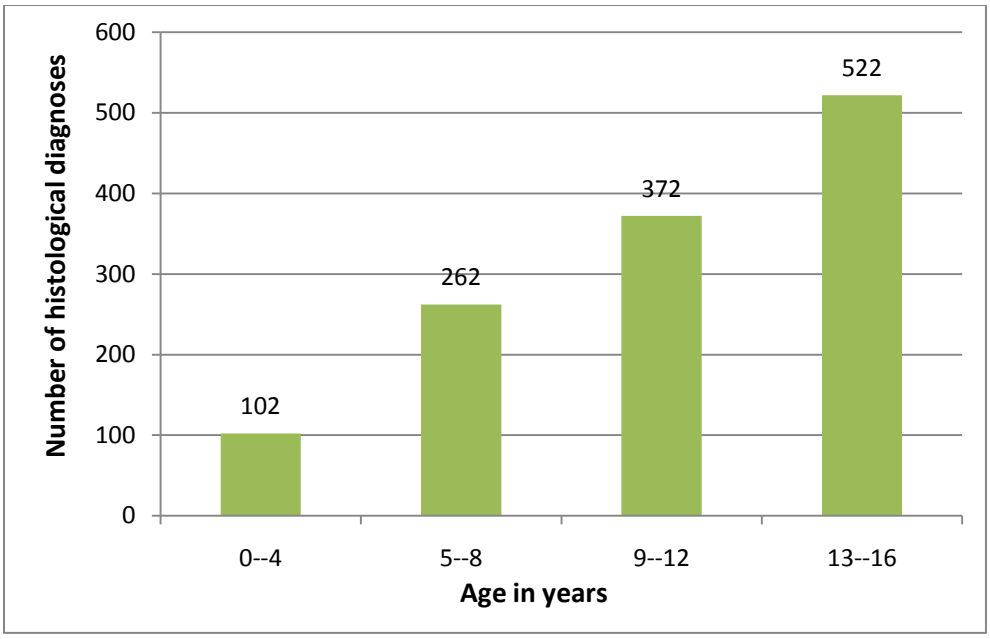

Figure 1: Number and distribution of 1258 cases of oral and maxillofacial pathology in children according to age.

The age distribution and frequency of the most common histopathological diagnoses in the paediatric population is depicted in Figure 2.

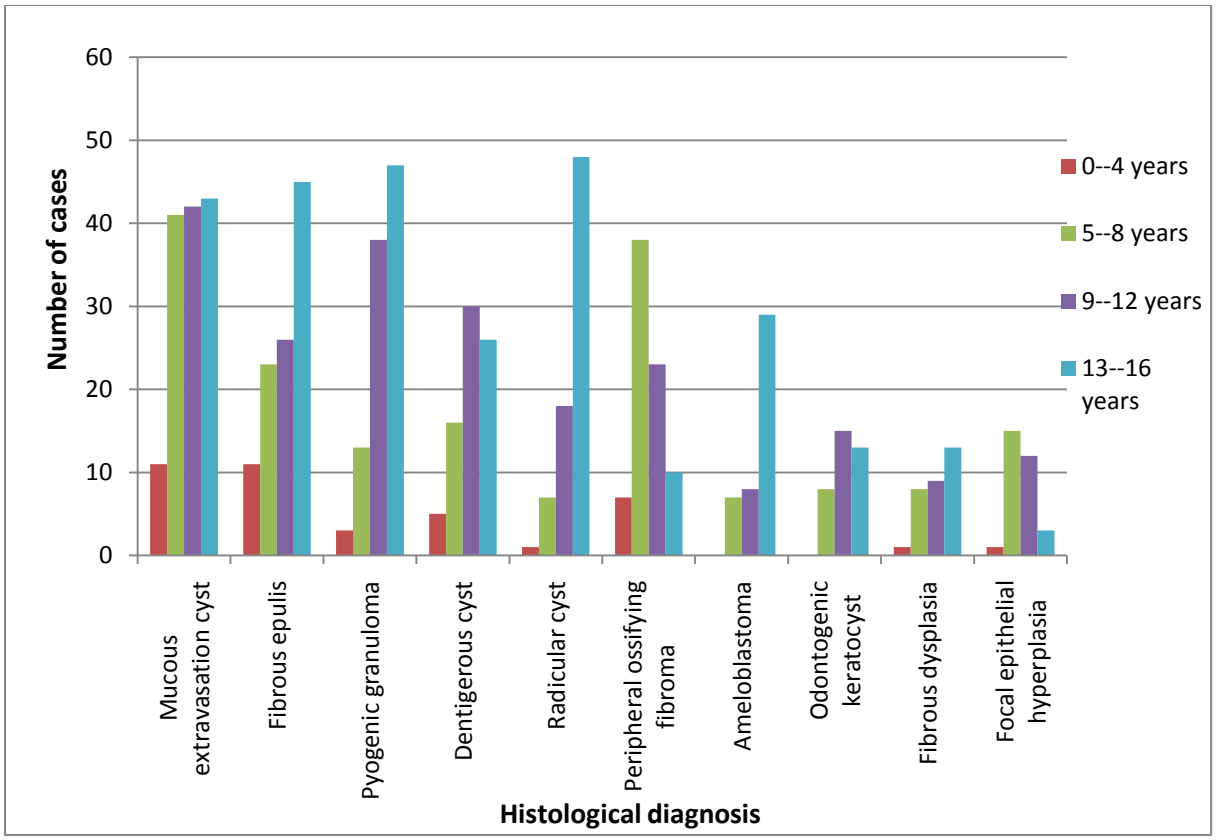

Figure 2: Age distribution and frequency of the 10 most common oral and maxillofacial histopathological diagnoses in children.

An increase in the frequency of the mucous extravasation cyst, fibrous epulis, pyogenic granuloma, radicular cyst, ameloblastoma and fibrous dysplasia was found with increase in the age of the patient. Exceptions to this finding were seen in the following lesions: dentigerous cyst, peripheral ossifying fibroma, odontogenic keratocyst and focal epithelial hyperplasia. The dentigerous cyst and odontogenic keratocyst showed a peak frequency in the 9-12 year age group while the peripheral ossifying fibroma and focal epithelial hyperplasia were diagnosed most commonly in children from 5 to 8 years of age.

5.2.2 Gender

598(47,5%) of the subjects were males and 635 were females (50.5%). The male to female ratio was 1:1,05. In 8 cases the gender of the patient was not provided.

The distribution of each age group as related to gender is illustrated in Figure 3.

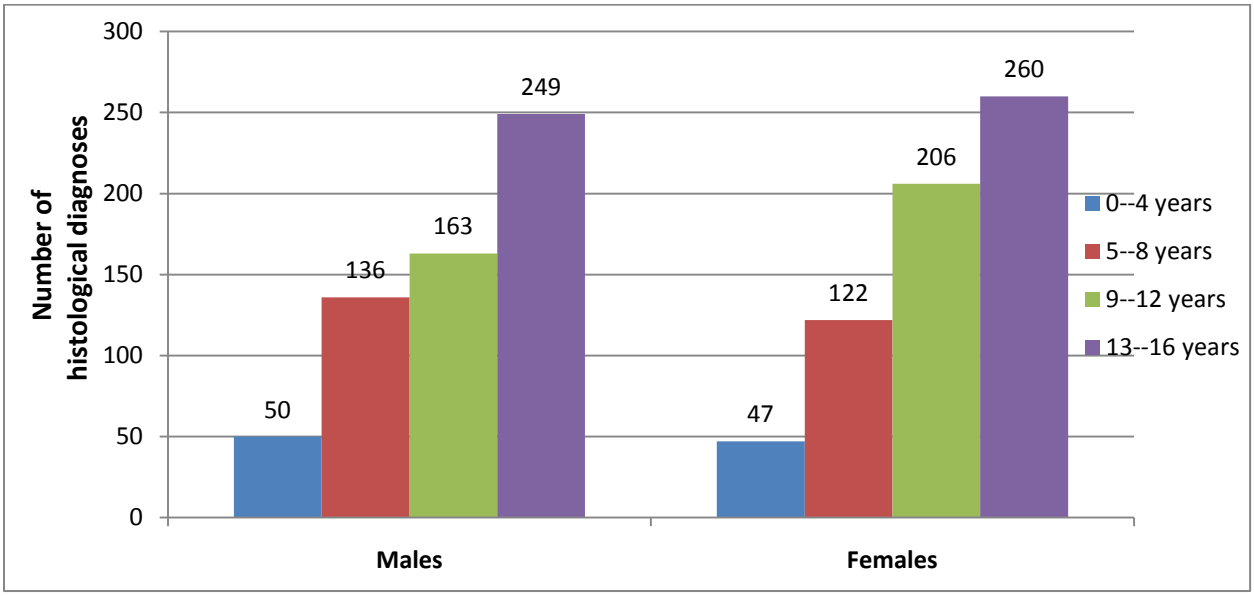

Figure 3: Age and gender distribution of oral and maxillofacial pathology in children.

Although a greater number of histopathological diagnoses were made in female than male patients from 9- to 16-years, the difference was not statistically significant (Fisher's exact two-tailed P value = 0,14). Conversely, also although not significantly different (Fisher's exact two-tailed P value = 0,81), up to the age of 8-years there were fewer biopsy specimens taken from girls.

5.3 Anatomical locations of oral and maxillofacial pathology

The most commonly affected intraoral sites of soft tissue lesions, in descending order, were the gingiva, buccal mucosa, tongue, lower lip, palate, upper lip and floor of the mouth. In 5,5% of cases the site of the lesion was not stated (Appendix 3). Malignant soft tissue tumours were most commonly observed on the gingiva, followed by the tongue and palate. Haemangiomas occurred more commonly on the buccal mucosa, followed by the lower lip, while the tongue was the most common site of occurrence of lymphangiomas (Appendix 3).

Collectively, odontogenic cysts and tumours occurred slightly more often in the mandible (n=152) than in the maxilla (n=145). Odontogenic cysts were, however, found to be more common in the maxilla (n=112), while benign odontogenic tumours were more commonly located in the mandible (n=64). Benign non-odontogenic tumours were also more prevalent in the mandible (n=20), while malignant non-odontogenic tumours were slightly more prevalent in the maxilla (n=10) (Appendix 4). Two cases of Burkitt's lymphoma showed involvement of both the maxilla and the mandible at the time of diagnosis. Dual pathologies were identified in 6 patients who presented with synchronous dentigerous cysts and odontogenic keratocysts (n=2), dentigerous cysts and radicular cysts (n=2) and radicular cysts and odontogenic keratocysts (n=2). In all 6 cases both cyst types occurred in the maxilla.

5.4 Types and frequencies of oral and maxillofacial pathology

5.4.1 Bone pathology

Pathology involving bone formed the largest category of all oral and maxillofacial pathologies with 524 cases, representing 41.7% of the total number of specimens. There were 311

odontogenic lesions, thereby constituting 59% of the total number of bone lesions, compared to 213 non-odontogenic lesions which constituted 40.6% of the category of bone lesions. The most commonly diagnosed odontogenic lesion was the dentigerous cyst (n= 79) followed closely by the radicular cyst (n=77). Overall, odontogenic cysts represented 16,6% (209/1258) of the total number of histological diagnoses. A total of 32 non-odontogenic cysts were diagnosed, 19 of which were nasopalatine duct cysts, 7 were solitary bone cysts and 6 were aneurysmal bone cysts. The ratio of odontogenic to non-odontogenic cysts was 6,5:1 (Figure 4, Appendix 5).

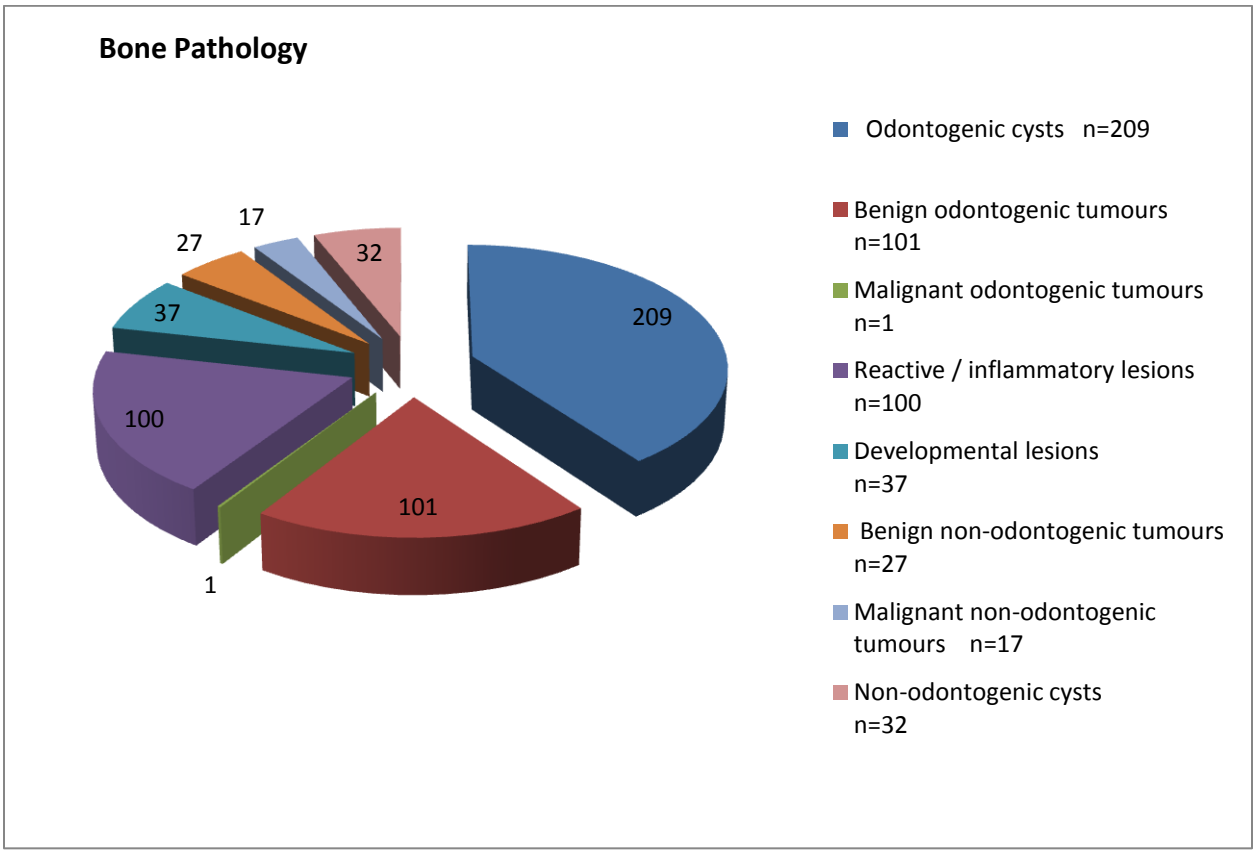

Figure 4: Types and frequencies of pathology affecting the jaw bones in children.

Odontogenic tumours accounted for 8,1% (102/1258) of the total number of histological diagnoses with the ameloblastoma (n=56) comprising 55,4% of all benign odontogenic tumours.

The most commonly diagnosed non-odontogenic lesion was fibrous dysplasia (n=31), which represented 6,2% of all bone lesions. Ossifying fibroma (n=18) was the most commonly diagnosed benign non-odontogenic neoplasm of bone. The ratio of benign odontogenic to benign non-odontogenic tumours of bone was 3,7:1. Burkitt's lymphoma (n=9) and osteosarcoma (n=6) accounted for 88,2% of all malignant non-odontogenic tumours. 19% of bone pathologies were reactive / inflammatory in nature and consisted predominantly of proliferative periostitis (n=22), chronic suppurative osteomyelitis (n=21) and periapical granuloma (n=21) (Appendix 5).

5.4.2 Soft tissue pathology

Soft tissue pathology formed the second largest category with 398 cases representing 31,6% of the total number of histological diagnoses (Figure 5, Appendix 6).

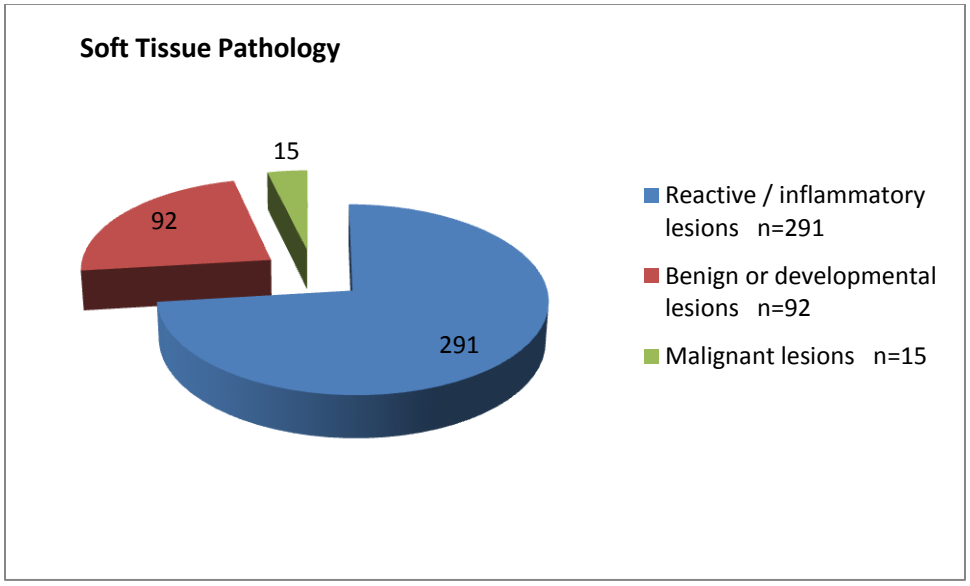

Figure 5: Types and frequencies of oral and perioral soft tissue pathology in children.

Reactive / inflammatory type lesions represented the vast majority (73,1%) of soft tissue lesions and included fibroepithelial polyps (n=105), pyogenic granulomas (n=101), peripheral ossifying

fibromas (n=50) and peripheral giant cell granulomas (n=12). Vascular lesions, in particular haemangioma and lymphangioma, comprised 1,7% and 1% of the total number of histological diagnoses respectively. Sarcomas accounted for 3,8% of all soft tissue lesions and included 8 cases of rhabdomyosarcoma, 4 cases of Kaposi's sarcoma, 2 fibrosarcomas and 1 case of an alveolar soft part sarcoma which was found on the tongue of a 4-year-old boy.

5.4.3 Salivary gland pathology

Salivary gland pathology accounted for 18% of the total number of histological diagnoses (Figure 6).

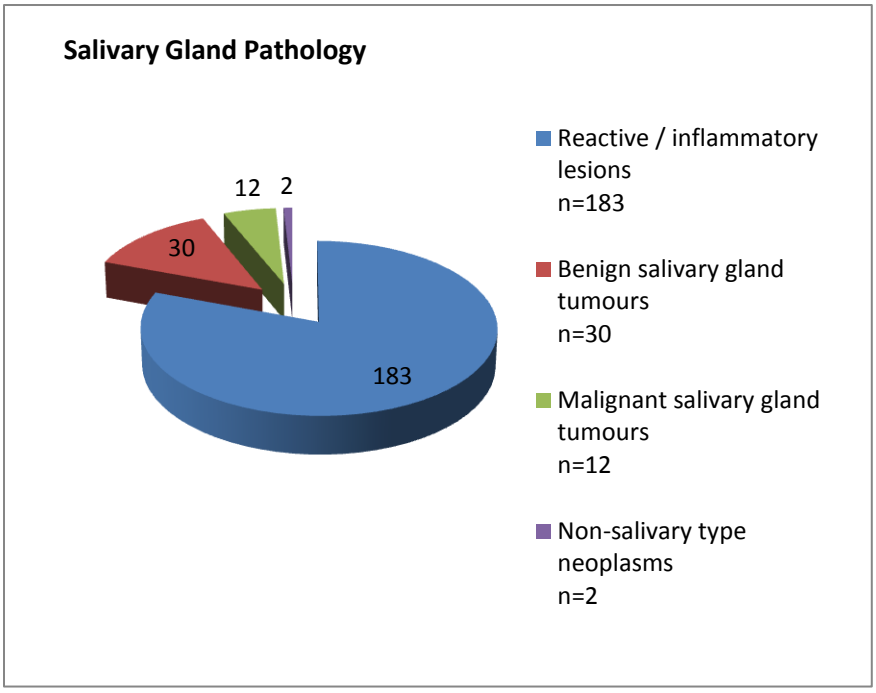

Figure 6: Types and frequencies of salivary gland lesions in children.

Mucoceles (extravasation and retention type) constituted 70% of all salivary gland lesions with 137 mucous extravasation cysts, 18 ranulas and 4 mucous retention cysts. The mucous extravasation cyst was also the most commonly diagnosed lesion within this study, comprising 10,9% of the total number of diagnoses. Tumours of the salivary glands accounted for 19% of all salivary gland pathology. There were 25 cases of pleomorphic adenoma and 5 cases of myoepithelioma. 3% of all salivary gland lesions were malignant, with 7 cases of mucoepidermoid carcinoma, 2 cases of acinic cell carcinoma and 3 cases of adenocarcinoma (not otherwise specified) (Appendix 7). The mean age of occurrence of salivary tumours was 12,8 years (median=13 years) with a three-fold predilection for occurrence in females. There was a slightly higher occurrence of malignant neoplasms (58,3%) in the major salivary glands (n=7) compared to the minor glands (n=5) (Appendix 8).

5.4.4 Oral mucosal pathology

Pathology of the oral mucosa accounted for 8,9% of the total number of histological diagnoses . Nearly two-thirds of all oral mucosal lesions were viral-induced lesions and included 31 cases of focal epithelial hyperplasia and 27 cases of squamous papilloma (Appendix 9). There were 6 cases of squamous cell carcinoma, which showed equal distribution among males and females and a mean age at referral of 10-years (Appendix 10).

5.4.5 Non-carious lesions of dental hard tissue

The diagnostic category with the smallest number of specimens was pathology related to developmental abnormalities of enamel (dens invaginatus n=3) and constituted 0.2% of the total number of specimens. This may be because most of these diagnoses are made clinically, with unfortunately very few specimens being submitted for histopathological examination.

5.5 Distribution of odontogenic versus non-odontogenic tumours of bone in South African children according to the developmental status of the dentition

With the aid of a 2x2 contingency table the frequency of odontogenic versus non-odontogenic tumours of bone were compared in children above and ≤12-years of age, i.e. in the early permanent dentition and in the mixed dentition period respectively. The data is represented in Table 1.

Table 1: Distribution of odontogenic and non-odontogenic tumours of bone in children above and ≤ 12-years of age.

	Odontogenic tumours of bone	**Non-odontogenic tumours of bone**	*Total*
Age group			
> 12-years	68	18	86
≤ 12-years	34	26	60
Total	102	44	146

Statistical analysis of the above data by means of the Fisher's exact test, confirmed that odontogenic tumours were significantly more common in children older than 12-years of age (*P*-value = 0,0057). The data also shows that in both age groups odontogenic tumours significantly outnumbered non-odontogenic tumours of the jaw bones.

5.6 Types and age distribution of malignant neoplasms of the oral and maxillofacial region in South African children

A total of 52 malignant diagnoses were made comprising 4,1% of the total number of histological diagnoses (Appendix 10). The most common malignancy was Burkitt's lymphoma (n=9), followed closely by rhabdomyosarcoma (n=8) and mucoepidermoid carcinoma. The mean age of the patients with malignant tumours was 9,3 years (standard deviation=4,14years), with a range of 1 year to 15 years. Malignant tumours were most common in the 9-12 year age group studied. Although the smallest number of biopsy specimens were obtained from children younger than 5-years of age, the likelihood of a malignant diagnosis was substantially higher (9%) than in older children where the frequency of a malignant diagnosis was in the order of 3,8%, 4,8% and 2,9% in the 5-8-, 9-12- and 13-16 year age groups respectively (Figure 7).

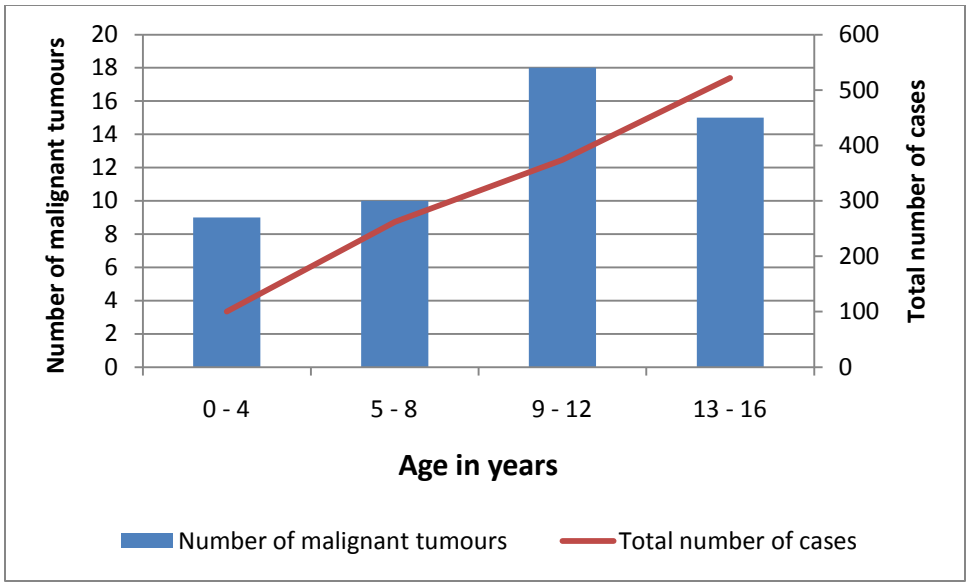

Figure 7: Distribution of malignant neoplasms according to age and in relation to the total number of cases studied in the four age groups.

CHAPTER SIX

6.0 DISCUSSION

The distribution of oral and maxillofacial pathology among the paediatric population has been studied in various countries around the world. Different epidemiological details of children harbouring orofacial disease, as diagnosed on biopsy, have been analysed in these studies. Such studies are, however, few from the developing countries of sub-Saharan Africa and in this particular region have thus far only emanated from Nigeria[11] and Tanzania.[21] The current study analysed epidemiological data, obtained from oral and maxillofacial histopathology reports, in a South African paediatric population. The following is a discussion of the findings on each study objective, which includes a comparison with other studies.

6.1 Frequency of oral and maxillofacial pathology in the paediatric population

Previous studies investigating the occurrence of oral and maxillofacial lesions in paediatric patients showed that the number of paediatric biopsies generally accounts for less than 10% of all oral histopathology biopsies.[7-10,17,20,28,29] There are, however, three studies from different parts of Nigeria that report much higher frequencies.[11-13] In these studies, that were conducted over an average period of 11 years, children up to the age of 16 years accounted for 16,2%-20,2% of the total oral biopsies.[11-13] The current review of the files at the University of the Witwatersrand's Division of Oral Pathology, over a 20-year period (1987-2007), revealed that of a total of 19,369 biopsies, 1258 (6,5%) were from children and adolescents up to the age of 16 years. While this figure is comparable with the general trend that is described in most studies, it is much lower than the values reported from Nigeria.[11-13] Factors that may contribute to the disparity between

these studies include the geographical region and the type of institution where the studies were conducted as well as the genetic background of the populations studied. Of these factors, it is surmised that the difference in population densities between Nigeria (1997 population estimate = 107-118 million, 45% of the population being under 15 years of age) and South Africa (1997 population estimate = 42,5 million, 33% of the population being under 15 years of age) is the most probable source for this discrepancy between the two countries.[56]

While some authors believe that the relative frequency of oral and perioral tumours and tumour-like lesions is higher in the African population than in other racial groups,[13,46] others doubt this postulate.[28] The relatively low frequency of oral biopsies from South African children when compared to children in other parts of Africa also tends to make the aforementioned premise tenuous. It is conceded that one of the limitations of the present study is the lack of data on the racial constitution of the population studied, which precludes an emphatic deduction with regards the influence of race on the frequency of oral biopsies from children in South Africa. It is, nevertheless, noteworthy that despite South Africa being ethnically diverse, with the largest European, Indian, and racially mixed communities in Africa; 79,5% of the South African population is of African descent.

6.2 Age distribution, gender distribution and anatomical location in relation to paediatric oral and maxillofacial pathology

6.2.1 Age

The mean age of study subjects in the present study was 10,7 years. In keeping with previous work,[7] children below 5-years of age were the least affected while a progressive increase in frequency of lesions with increasing age was noted (Figure 1).

The findings of this study further show that different types of lesions affect different ages and age groups differently. Of the 10 most commonly diagnosed lesions, the mucous extravasation cyst, fibrous epulis, pyogenic granuloma, radicular cyst, ameloblastoma and fibrous dysplasia were found to be commonest among children aged between 13 years and 16 years. These lesions also showed a progressive increase with increase in the age of the patient (Figure 2). Also in agreement with most previous series from other countries the mucous extravasation cyst was by far the most common lesion in all the age groups that were studied (Figure 2).[7,8,15,16,18]

In the present study, the following lesions were only diagnosed in patients over the age of 8-years; pleomorphic adenoma, myoepithelioma, acinic cell carcinoma, multicystic ameloblastoma, odontomes, ameloblastic fibroma, calcifying odontogenic cyst, myxofibroma, adenomatoid odontogenic tumour and solitary bone cyst. Most papers regarding salivary gland tumours in children and adolescents, have shown that all salivary gland epithelial tumours are more common in the second decade of life, their occurrence being exceptionally rare in the first decade.[33] In accordance with other authors' experiences it was also found that odontogenic tumours were significantly more common in children over 12 years of age (Table 1), despite the fact that crown formation is completed by 4- to 5-years of age in most of the permanent teeth.[9,32] This finding militates against origin of odontogenic tumours from the developing tooth germ and strengthens the hypothesis that the majority of odontogenic tumors arise from quiescent remnants

of the tooth germ.[32] Presentation of these tumours seven years after completion of teeth crowns could further be due to the slow growth rate of these benign tumours, which originate intra-medullary and they may therefore remain undetected for a number of years.

The mean age of the patients with malignant tumours in the present study was 9,3 years (standard deviation=4,14years). Malignant tumours were most common in the 9-12 year age group studied (Figure 8). This is in keeping with studies from Nigeria, which show the distribution of malignant tumours is greater from the second decade of life.[11,27,57] Contrary to these findings, in a study on orofacial tumours in Libyan children and adolescents, Elarbi *et al.*[10] found the majority of malignant tumours in their youngest (0-5 year) patient age group. Patients in the latter age group were also among those Israeli children wherein the number of malignant tumours was greatest.[28] The malignant tumours were almost evenly distributed among Japanese children up to the age of 15 years.[9] In the present work, although the smallest number of total biopsy specimens were obtained from children younger than 5 years of age, the likelihood of a malignant diagnosis was substantially higher (8,7%) than in older children where the frequency of a malignant diagnosis was in the order of 2,6%, 4,8% and 2,0% in the 5-8, 9-12 and 13-16 year age groups respectively (Figure 8).

6.2.2 Gender

In the present work, although there was a predominance of biopsies from male patients under the age of 9 years (Figure 3), overall there were more females than males, with a female to male ratio of 1,06:1. Other studies, however, show an overall male predominance among children with oral lesions that were biopsied.[7,11,13,27,32] Also contrary to most studies, in the present survey a

larger number of malignant tumours were found in females (n=28) than in males (n=22) (Appendix 10). This finding may be partially attributed to the fact that more females were afflicted by rhabdomyosarcoma, the most common sarcoma in this study and by salivary gland adenocarcinomas. The total number of cases in each category of malignant lesions is, however, too small to draw definitive conclusions for this gender discrepancy between the present study and earlier work.

6.2.3 Anatomical location

In contradistinction to the studies of Al-Khateeb *et al.*,[32] Sato *et al.* [9] and Bhaskar *et al.*,[55] on oral and maxillofacial biopsies in children, where the lower lip and tongue were recorded as the commonly biopsied sites, we found that the number of bone biopsies (n=502) (Appendix 4) exceeded those of soft tissue (n=298) (Appendix 3) and mucosa (n=112) combined, with the maxilla being the most commonly affected site followed by the mandible (Appendix 4). This finding in turn corresponded with the combined higher frequency of odontogenic cysts and odontogenic tumours, found in this study, when compared with soft tissue and mucosal pathology. In agreement with previous work, the gingiva, lower lip and tongue were the most common sites biopsied outside bone (Appendix 3).[9,32,55]

6.3 Types and frequencies of paediatric oral and maxillofacial pathology

Among the most common diagnoses in the present study (Figure 2), fibrous epulis, dentigerous cyst, odontogenic keratocyst and ameloblastoma showed a higher frequency than studies from Europe[7] and South America.[20] The relevant findings are summarised in Table 2.

Table 2: Most common diagnoses in the following categories: salivary gland pathology, fibrogranulomatous lesions, odontogenic cysts and tumours and benign fibro-osseous lesions. A comparison of the present findings with previous work.

Lesion	**Number of cases**			**% of total specimens**		
	Present study	Jones *et al.*[7]	Keszler *et al.*[20]	Present study	Jones *et al.*[7]	Keszler *et al.*[20]
1. Mucocele	137	735	76	10.9	16,7	6,0
2. Fibrous epulis	105	192	55	8.3	4,4	4,3
3. Dentigerous cyst	79	157	68	**6.1**	3,6	5,3
4. Radicular cyst	77	238	148	5.9	5,4	11,5
5. Ameloblastoma	56	9	8	**3.5**	< 1,0	<1,0
6. Odontogenic keratocyst	36	71	12	**2.9**	1,6	<1,0
7. Fibrous dysplasia	31	16	33	2.5	<1.0	2,6

The higher frequency of ameloblastoma and odontogenic keratocyst in this study, compared to non-African studies, supports the contention that genetic factors probably play a key role in the development of pathologies related to the odontogenic apparatus.[11]

6.3.1 Bone pathology

The vast majority of biopsied lesions in this study were derived from bone. This is an additional indication that pathology involving bone is central to this particular field of diagnostic histopathology since most diagnoses in other studies were also of lesions situated within the jaws and/or facial bones.[7,17,25,27] In harmony with at least 6 other studies, [8,17,18,19,25,29] dentigerous cysts were the most frequently encountered odontogenic cyst in our paediatric population. This was, however, followed closely by the radicular cyst in the present study (Table 2). Studies conducted in the United Kingdom,[7] South America[20]and the United States of America,[15] show that radicular cysts are by far the most common odontogenic cysts in children. The reason for this difference may relate to the frequency of caries between different countries. A DMFT index of 1,5 has been reported for Africans while that for Americans and Europeans were 3,5 and 2,5 respectively.[58]

There is a notable difference in the frequency of occurrence of the nasopalatine duct cyst among the paediatric population at hand as opposed to other studies. In the current survey, the nasopalatine duct cyst comprised almost 60% of all non-odontogenic cysts (Appendix 5) while Jones *et al.*[7] showed a frequency of 25% in their group of non-odontogenic cysts. There are only two other studies of this nature wherein the authors of both papers report only one case each in surveys of 1251 and 534 cases respectively.[8,25] This finding may indicate a specific geographic pattern of localisation for the nasopalatine duct cyst when it occurs in young individuals.

Although higher than in Western countries,[7] a substantially lower frequency rate of odontogenic tumours (8,1%) was documented in this study, compared to some African and Asian studies, which report frequency rates as high as 25,9% for about the same age group.[9,11] Another point of divergence between the South African population studied and those of other African children is

the striking difference in the predominant histological type of ameloblastoma. In a comprehensive literature review on ameloblastoma in children, it emerged that in African children the ameloblastoma more closely resemble the adult patterns of ameloblastoma in their countries with only 19,5% being unicystic.[59] In Western children, however, 74.3% were unicystic.[59] The findings of the present study show a closer association with the Western racial group since it was found that unicystic ameloblastomas comprised 78,6% of all ameloblastomas occurring during childhood and early adolescence. Rather than reflecting a true genetic basis, it is possible that many of the African cases are multicystic at the time of diagnosis as a result of late diagnosis.[51] Future studies are, however, needed to investigate whether the multicystic ameloblastoma in children represents a continuum in development from luminal unicystic ameloblastoma with mural invasion and eventual bone invasion as a multicystic or solid ameloblastoma.

In agreement with other studies from sub-saharan Africa,[11,13] we also found a higher frequency of ameloblastoma (55,4%) compared to other odontogenic tumours. In line with recent studies there were fewer non-odontogenic than odontogenic paediatric jaw bone tumours,[10,17] with a calculated ratio of 1:3,7 in this study, fibrous dysplasia being the most frequently diagnosed benign non-odontogenic lesion of bone (Appendix 4).

Sequestra / chronic suppurative osteomyelitis were rarely documented in most surveys of biopsy material obtained from children. A frequency of 1,83% of histologically confirmed cases was recorded in this study, which is slightly lower than the frequency rates reported in two earlier studies among Thai and Argentinean children respectively.[25,20] In keeping with the general

population we found that in children chronic suppurative osteomyelitis also shows a predilection for the mandible (Appendix 4) .

6.3.2 Soft tissue pathology

The tumour-like fibrogranulomatous lesions (pyogenic granuloma, fibroepithelial polyp, epulis, peripheral cemento-ossifying fibroma), represented the majority (73,1%) of lesions of connective tissue (Appendix 6). In the work by Elarbi *et al.*[10] patients in the 10 to 14 year age group accounted for most of these lesions. This is corroborated by the mean age of 11,2 years that was found in this study. Although females were found to outnumber males for this particular group of lesions, this was only by a narrow margin (1:1,3 male:female ratio) in this study and hence does not entirely support a role for hormones being responsible for these lesions as was previously suggested.[10]

Vascular malformations, in particular haemangioma and lymphangioma, comprised 1,8% and 1,0% of the total specimens respectively (Appendix 6). This is within the frequency range reported by most authors except Al-Khateeb *et al.*[32] and Sato *et al.*[9] who pointed out the tendency of the haemangioma as the most frequent paediatric diagnosis in the Jordanian and Japanese populations respectively (+/- 27% of total specimens). Sato *et al.*[9] found the tongue was the most common site of haemangiomas, while Bhaskar *et al.*[55] and Jones *et al.*[7] found the lip to be the most common site of occurrence.

Rhabdomyosarcoma was the most common malignant soft tissue tumour and accounted for 15,4% of all childhood malignancies in this study (Appendix 10). This is in agreement with the

previously established high percentage of rhabdomyosarcoma among malignant head and neck tumours in children.[9,28]

6.3.3 Salivary gland pathology

Considering the salivary gland lesion group, in previous studies the mucocele represented up to 89,2% of all salivary gland biopsies revealing a considerable occurrence in paediatric populations.[8,15,17,18] Mucous extravasation cysts comprised the largest single diagnostic group in this study, accounting for over 10% of the total number of biopsy specimens (Appendix 7). Although frequent in children and adolescents, until recently no studies of mucocele in this specific population have been performed. During a 16-year period, Nico *et al.*[60] found 36 of 104 patients with salivary mucoceles were aged 15-years old or younger (34,6%) and tongue lesions (mucocele of the glands of Blandin-Nuhn) were more prevalent in children than in adults.

Although salivary tumours are rare within paediatric populations, a 1:1 ratio of benign to malignant salivary tumours has generally been reported.[7,33] In previous studies,[7,33] mucoepidermoid carcinoma was the most common malignant salivary gland neoplasm in children and the present results are consistent with this (Appendix 8). There is, however, discordance in the ratio of benign to malignant salivary tumours that evinced from this study compared to the literature. Of the 42 epithelial salivary gland tumours in this study, 30 (71,4%) were benign and 12 (28,6%) malignant yielding a 2,5:1 ratio of benign to malignant salivary tumours. Another notable difference is the site distribution of pleomorphic adenoma. Although the majority of authors describe the parotid gland as the most common site for pleomorphic adenoma,[34,61] the present study describes a high frequency of pleomorphic adenoma in the

submandibular glands, which was the most common site for these tumours in children (Appendix 8). Future studies are required to determine whether the differences in the occurrence of these tumours may be associated with geographically-related environmental factors, genetic differences, race and or differences in biological properties of putative causative organisms such as Epstein-Barr virus.

6.3.4 Oral mucosal pathology

Most reports indicate Human Papilloma Virus (HPV)-induced benign squamo-proliferative lesions as the most frequently biopsied oral lesion of infectious origin with squamous papilloma being the most frequently diagnosed lesion in this category.[7,9,15,16,17,18,25,30,32] We found a slightly higher occurrence of focal epithelial hyperplasia (n=31; 2,46% of total specimens) than squamous papilloma (n=27; 2,14% of total specimens), however, the difference was not highly significant (Appendix 9). The comparatively lower percentage (0,4%) of squamous papilloma in southern Taiwanese and Libyan children and adolescents remains unexplained, but the authors speculate that it may be due to geographic variations.[8,10]

Oral squamous cell carcinoma is reported to be rare in children under 18-years and extremely rare in children less than 10 years.[62] In the present study 3 cases were seen in children below 10 years of age. Four of the six cases were discovered at extra-lingual sites (Appendix 10). Possible predisposing conditions were, however, not analysed in this study.

6.3.5 Non-carious lesions of dental hard tissue

Pathology related to the dental hard tissues (excluding caries) constituted the smallest number of specimens and consisted of 3 cases of dens invaginatus. This contrasts with the myriad of abnormalities of enamel and dentine (n=231) including cases of hypophosphatasia, vitamin-D-resistant rickets, amelogenesis imperfecta and dentinogenesis imperfecta that were submitted for histological evaluation at an Oral Pathology diagnostic service in the United Kingdom.[7] Furthermore, of the previously reported data only two other studies included a sub-classification for dental pathology.[19,20] Epidemiologically, however, non-carious lesions of dental hard tissue are probably grossly underestimated with clinical diagnoses of these lesions masking the true extent of these conditions.

CHAPTER SEVEN

7.0 CONCLUSIONS

- Less than 10% of all oral and maxillofacial cases submitted for histopathological report were from children younger than 16 years.
- The average age of children with histologically confirmed disease in the oral and/or maxillofacial region was 10,7 years.
- The older the child the higher was the likelihood of being diagnosed with oral and/or maxillofacial pathology. A child older than 9 years was 2,5 times more likely to have a histologically confirmed disease in the oral and/or maxillofacial region.
- Although the smallest number of biopsy specimens was obtained from children younger than 5 years of age, the likelihood of a malignant diagnosis was substantially higher than in older children.
- There was a slight female predominance amongst children with oral and/or maxillofacial pathology.
- The most common histological diagnoses, in order of decreasing frequency, were mucous extravasation cyst (extravasation mucocele), fibrous epulis, pyogenic granuloma, dentigerous cyst, radicular cyst, ameloblastoma, peripheral ossifying fibroma, odontogenic keratocyst, fibrous dysplasia and focal epithelial hyperplasia.
- The majority of lesions were benign; 4,13% of cases comprised malignant lesions.

- The number of bone biopsies exceeded those of mucosa, soft tissue and salivary gland with the maxilla being more commonly affected than the mandible.
- Odontogenic tumours showed a significantly higher frequency in the post-mixed dentition period.
- A higher frequency of unicystic ameloblastoma than in the literature was noted.

7.1 Limitations of the study

- The results do not represent the actual frequency of oral disease in children, but simply the relative frequency of histologically diagnosed oral and maxillofacial lesions over a 20-year period.
- There is no data on ethnicity within this study, thereby precluding definitive statements regarding the racial predilection for the various types of oral and maxillofacial lesions.
- Treatment modalities and patient follow-up were not evaluated but is presently viewed as the potential subject of a future study.

APPENDIX 1: Data collection sheet

CASE NUMBER	AGE	GENDER	ANATOMICAL LOCATION	HISTOLOGICAL DIAGNOSIS
1				
2				
3				
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21…1258				

APPENDIX 2: Ethics committee clearance certificate

APPENDIX 3: Anatomical locations of intraoral soft tissue lesions

	Lower lip	Upper lip	Floor of mouth	Gingiva	Buccal mucosa	Palate	Tongue	Site not stated
Reactive / inflammatory lesions								
Pyogenic granuloma	22	8	1	28	8	8	11	15
Fibrous epulis / fibroepithelial polyp	4	5	0	39	29	7	19	2
Peripheral ossifying fibroma	0	0	0	43	1	6	0	0
Peripheral odontogenic fibroma	0	0	0	5	1	0	0	0
Peripheral giant cell granuloma	0	0	0	11	0	1	0	0
Foreign body granuloma	2	0	0	0	0	0	0	0
Gingival fibromatosis	0	0	0	4	0	0	0	0
Chronic hyperplastic gingivitis	0	0	0	11	0	0	0	0
Benign / developmental lesions								
Lymphangioma	0	0	2	2	1	2	6	0
Haemangioma	4	3	1	3	7	2	1	1
Lipoma	1	1	0	0	5	0	3	0
Neurofibroma	0	1	0	2	3	0	0	2
Schwannoma	0	0	1	0	0	0	1	0
Traumatic neuroma	0	0	0	0	0	0	1	0
Granular cell tumour	0	1	0	0	0	0	0	0
Myofibroma / myofibromatosis	0	0	0	1	2	0	0	0
Infantile fibromatosis	0	0	0	0	0	0	0	1
Nodular fasciitis	1	0	0	3	1	0	0	0
Benign fibrous histiocytoma	1	0	0	1	0	0	0	0
Juvenile xanthogranuloma	0	1	0	0	1	0	0	0
Leiomyoma	0	1	0	0	0	0	0	0
Mesenchymal hamartoma	0	0	0	0	1	0	1	0
Congenital epulis	0	0	0	4	0	0	0	0
Dermoid cyst	0	0	4	0	0	0	0	0
Epithelial inclusion cyst	0	1	1	0	0	2	1	0
Lymphoepithelial cyst	0	0	1	0	0	0	0	0
Cyst of the incisive papilla	0	0	0	0	0	1	0	0
Anterior median lingual cyst	0	0	0	0	0	0	1	0
Melanotic neuroectodermal tumour of infancy	0	0	0	3	0	0	0	0
Malignant lesions								
Rhabdomyosarcoma	1	0	0	3	1	1	1	1
Kaposi's sarcoma	0	0	0	1	0	1	2	0
Fibrosarcoma	0	0	0	1	0	1	0	0
Alveolar soft part sarcoma	0	0	0	0	0	0	1	0
TOTAL (n=398)	**36**	**22**	**11**	**165**	**61**	**32**	**49**	**22**

APPENDIX 4: Locations of odontogenic and non-odontogenic bone lesions

	Mandible	Maxilla	Site not stated
Odontogenic cysts (n=209)			
Odontogenic keratocyst	20	16	0
Radicular cyst	26	46	5
Dentigerous cyst	36	42	1
Eruption cyst	1	6	4
Calcifying odontogenic cyst	4	2	0
Total	87	112	10
Odontogenic tumours (n=102)			
Unicystic ameloblastoma	38	5	1
Multicystic ameloblastoma	11	1	0
Adenomatoid odontogenic tumour	2	15	1
Ameloblastic fibroma	0	2	0
Ameloblastic fibro-odontoma	2	1	0
Odontome	8	6	2
Myxofibroma	3	2	0
Cementoblastoma	1	0	0
Odontogenic Carcinoma	0	1	0
Total	65	33	4
Reactive / inflammatory lesions (n=79)			
Central giant cell granuloma	8	8	1
Proliferative periostitis	22	0	0
Chronic suppurative osteomyelitis	13	8	0
Chronic osteitis	6	0	0
Tuberculous osteomyelitis	3	0	0
Temperomandibular joint arthritis	4	0	0
Temperomandibular joint ankylosis	6	0	0
Total	62	16	1
Developmental lesions (n=37)			
Cherubism	4	1	1
Fibrous dysplasia	10	20	1
Total	14	21	2
Benign non-odontogenic tumours (n=27)			
Desmoplastic fibroma	5	1	0
Ossifying fibroma	12	6	0
Osteoma	2	0	0
Langerhans cell histiocytosis	1	0	0
Total	20	7	0
Malignant non-odontogenic tumours (n=19)			
Burkitt's lymphoma	5	4	2
Osteosarcoma	2	4	0
Plasmacytoma	0	2	0
Total	7	10	2
Non-odontogenic cysts (n=32)			
Nasopalatine duct cyst	0	19	0
Solitary bone cyst	7	0	0
Aneurysmal bone cyst	4	2	0
Total	11	21	0

APPENDIX 5: Types and frequencies of bone lesions

Histological diagnosis	Number of cases	% in relation to other bone lesions	% in relation to total number of specimens
Odontogenic cysts and tumours (n=311)			
Odontogenic cysts (n=209)			
Odontogenic keratocyst	36	6.87	2.86
Radicular cyst	77	14.12	6.12
Dentigerous cyst	79	14.69	6.28
Eruption cyst	11	2.10	0.87
Calcifying odontogenic cyst	6	1.15	0.48
Odontogenic tumours (n=102)			
Unicystic ameloblastoma	44	8.40	3.5
Multicystic ameloblastoma	12	2.29	0.95
Adenomatoid odontogenic tumour	18	3.44	1.43
Ameloblastic fibroma	2	0.38	0.16
Ameloblastic fibro-odontoma	3	0.57	0.24
Odontome	16	3.05	1.27
Myxofibroma	5	0.95	0.4
Cementoblastoma	1	0.19	0.08
Odontogenic carcinoma	1	0.19	0.08
Non-odontogenic lesions (n=213)			
Reactive / inflammatory lesions (n=100)			
Central giant cell granuloma	17	3.24	1.35
Proliferative periostitis	22	4.20	1.75
Chronic suppurative osteomyelitis	21	4.01	1.67
Periapical granuloma	21	4.01	1.67
Chronic osteitis	6	1.15	0.48
Tuberculous osteomyelitis	3	0.57	0.24
Temporomandibular joint arthritis	4	0.76	0.32
Temporomandibular joint ankylosis	6	1.15	0.48
Developmental lesions (n=37)			
Cherubism	6	1.15	0.48
Fibrous dysplasia	31	5.92	2.46
Benign non-odontogenic tumours (n=27)			
Desmoplastic fibroma	6	1.15	0.48
Ossifying fibroma	18	3.44	1.43
Osteoma	2	0.38	0.16
Langerhan's cell histiocytosis	1	0.19	0.08
Malignant non-odontogenic tumours (n=17)			
Burkitt's lymphoma	9	1.72	0.72
Osteosarcoma	6	1.15	0.48
Plasmacytoma	2	0.38	0.16
Non-odontogenic cysts (n=32)			
Nasopalatine duct cyst	19	3.63	1.51
Solitary bone cyst	7	1.34	0.56
Aneurysmal bone cyst	6	1.15	0.48

APPENDIX 6: Types and frequencies of soft tissue lesions

Histological diagnosis	Number of cases	% in relation to other soft tissue lesions	% in relation to total number of specimens
Reactive / Inflammatory lesions (n=291)			
Pyogenic granuloma	101	25.4	8.02
Fibrous epulis / fibroepithelial polyp	105	26.4	8.34
Peripheral ossifying fibroma	50	12.6	3.97
Peripheral odontogenic fibroma	6	1.5	0.48
Peripheral giant cell granuloma	12	3.0	0.95
Foreign body granuloma	2	0.5	0.16
Gingival fibromatosis	4	1.0	0.32
Chronic hyperplastic gingivitis	11	2.8	0.87
Benign, developmental or cystic lesions (n=92)			
Lymphangioma	13	3.3	1.03
Haemangioma	22	5.5	1.75
Lipoma	10	2.5	0.79
Neurofibroma	8	2.0	0.64
Schwannoma	2	0.5	0.16
Traumatic neuroma	1	0.3	0.08
Granular cell tumour	1	0.3	0.08
Myofibroma / myofibromatosis	3	0.8	0.24
Infantile fibromatosis	1	0.3	0.08
Nodular fasciitis	5	1.3	0.40
Benign fibrous histiocytoma	2	0.5	0.16
Juvenile xanthogranuloma	2	0.5	0.16
Leiomyoma	1	0.3	0.08
Mesenchymal hamartoma (mesenchymoma)	2	0.5	0.16
Congenital epulis	4	1.0	0.32
Dermoid cyst	4	1.0	0.32
Epithelial inclusion cyst	5	1.3	0.40
Oral lymphoepithelial cyst	1	0.3	0.08
Cyst of the incisive papilla	1	0.3	0.08
Anterior median lingual cyst	1	0.3	0.08
Melanotic neuroectodermal tumor of infancy	3	0.8	0.24
Malignant lesions (n=15)			
Rhabdomyosarcoma	8	2.0	0.64
Kaposi's sarcoma	4	1.0	0.32
Fibrosarcoma	2	0.5	0.16
Alveolar soft part sarcoma	1	0.3	0.08

APPENDIX 7: Types and frequencies of salivary gland lesions

Histological diagnosis	Number of cases	% in relation to other salivary gland lesions	% in relation to total number of specimens
Reactive/ Inflammatory lesions (n=183)			
Mucous extravasation cyst	137	60.4	10.88
Ranula	18	7.9	1.43
Mucous retention cyst	4	1.8	0.32
Recurrent parotitis	1	0.4	0.08
Non-specific chronic sialadenitis	11	4.6	0.87
Acute suppurative sialadenitis	5	2.2	0.40
Chronic sclerosing sialadenitis	4	1.8	0.32
Lymphoepithelial cyst	2	0.9	0.16
Adenomatoid hyperplasia of minor salivary glands	1	0.4	0.08
Benign salivary gland tumours (n=30)			
Pleomorphic adenoma	25	11	1.99
Myoepithelioma	5	2.2	0.40
Malignant salivary gland tumours (n=12)			
Mucoepidermoid carcinoma	7	3	0.56
Acinic cell carcinoma	2	0.9	0.16
Adenocarcinoma (Not Otherwise Specified)	3	1.3	0.24
Non-salivary type neoplasms (n=2)			
Plexiform neurofibroma	1	0.4	0.08
B-cell non-Hodgkin lymphoma	1	0.4	0.08

APPENDIX 8: Age, gender and site distribution of salivary gland tumours

Age (yr)	Gender	Anatomical location	Histological diagnosis
10	female	Palate	Pleomorphic adenoma
11	female	Palate	Pleomorphic adenoma
12	male	Palate	Pleomorphic adenoma
12	male	Palate	Pleomorphic adenoma
13	female	Palate	Pleomorphic adenoma
14	male	Palate	Pleomorphic adenoma
13	female	Palate	Pleomorphic adenoma
16	male	Submandibular gland	Pleomorphic adenoma
14	female	Buccal mucosa	Pleomorphic adenoma
14	female	Palate	Pleomorphic adenoma
14	female	Palate	Pleomorphic adenoma
9	male	Palate	Pleomorphic adenoma
12	female	Palate	Pleomorphic adenoma
16	male	Palate	Pleomorphic adenoma
13	female	Palate	Pleomorphic adenoma
13	female	Parotid gland	Pleomorphic adenoma
15	female	Submandibular gland	Pleomorphic adenoma
11	female	Submandibular gland	Pleomorphic adenoma
15	female	Submandibular gland	Pleomorphic adenoma
13	female	Submandibular gland	Pleomorphic adenoma
15	male	Parotid gland	Pleomorphic adenoma
14	female	Parotid gland	Pleomorphic adenoma
16	male	Parotid gland	Pleomorphic adenoma
16	male	Submandibular gland	Pleomorphic adenoma
14	female	Submandibular gland	Pleomorphic adenoma
14	female	Palate	Myoepithelioma
11	female	Palate	Myoepithelioma
14	male	Palate	Myoepithelioma
14	female	Palate	Myoepithelioma
12	female	Palate	Myoepithelioma
14	female	Palate	Mucoepidermoid carcinoma
9	female	Palate	Mucoepidermoid carcinoma
8	female	Parotid gland	Mucoepidermoid carcinoma
13	female	Parotid gland	Mucoepidermoid carcinoma
15	female	Parotid gland	Mucoepidermoid carcinoma
15	female	Buccal mucosa	Mucoepidermoid carcinoma
15	male	Submandibular gland	Mucoepidermoid carcinoma
6	female	Palate	Adenocarcinoma
11	female	Palate	Adenocarcinoma
9	female	Submandibular gland	Adenocarcinoma
12	female	Parotid gland	Acinic cell carcinoma
12	female	Submandibular gland	Acinic cell carcinoma

APPENDIX 9: Types and frequencies of oral mucosal lesions

Histological diagnosis	**Number of cases**	**% in relation to other oral mucosal lesions**	**% in relation to total number of specimens**
Reactive / Inflammatory lesions (n=16)			
Erythema multiforme	1	0.89	0.08
Lichen planus	1	0.89	0.08
Inflammatory papillary hyperplasia	1	0.89	0.08
Geographic tongue	1	0.89	0.08
Non-specific chronic ulceration	12	10.71	0.95
Viral associated lesions of oral mucosa (n=65)			
Squamous papilloma	27	24.11	2.14
Verruca vulgaris	4	3.57	0.32
Focal epithelial hyperplasia	31	27.68	2.46
Herpes simplex virus oral ulceration	2	1.79	0.16
Cytomegalovirus oral ulceration	1	0.89	0.08
Fungal associated lesions of the oral mucosa (n=16)			
Oral candidiasis	16	14.29	1.27
Bacterial associated lesions of the oral mucosa (n=5)			
Secondary syphilis	1	0.89	0.08
Tuberculosis	4	3.57	0.32
Benign / Hamartomatous lesions (n=4)			
Benign intramucosal naevus	1	0.89	0.08
Oral melanotic macule	1	0.89	0.08
Odontogenic gingival hamartoma	2	1.79	0.16
Malignant lesions (n=6)			
Squamous cell carcinoma	6	5.36	0.48

APPENDIX 10: Age, gender and site distribution of malignant oral and maxillofacial tumours

Age (yr)	Gender	Anatomical location	Histological diagnosis
12	female	Parotid gland	Acinic cell carcinoma
12	female	Submandibular gland	Acinic cell carcinoma
6	female	Palate	Adenocarcinoma
11	female	Palate	Adenocarcinoma
9	female	Submandibular gland	Adenocarcinoma
4	male	Tongue	Alveolar soft part sarcoma
11	male	Mandible	Burkitt's lymphoma
5	female	Mandible and maxilla	Burkitt's lymphoma
13	male	Maxilla	Burkitt's lymphoma
6	female	Mandible	Burkitt's lymphoma
5	female	Maxilla	Burkitt's lymphoma
10	male	Not stated	Burkitt's lymphoma
2	male	Mandible and maxilla	Burkitt's lymphoma
10	male	Mandible	Burkitt's lymphoma
3	male	Not stated	Burkitt's lymphoma
15	female	Mandible	Chondroblastic osteosarcoma
13	female	Palate	Fibrosarcoma
11	female	Maxilla	Fibrosarcoma
4	male	Gingiva	Kaposi's sarcoma
7	female	Tongue	Kaposi's sarcoma
10	male	Tongue	Kaposi's Sarcoma
14	female	Palate	Kaposis sarcoma
14	female	Palate	Mucoepidermoid carcinoma
9	female	Palate	Mucoepidermoid carcinoma
8	female	Parotid gland	Mucoepidermoid carcinoma
13	female	Parotid gland	Mucoepidermoid carcinoma
15	female	Parotid gland	Mucoepidermoid carcinoma
15	female	Buccal mucosa	Mucoepidermoid carcinoma
15	male	Submandibular gland	Mucoepidermoid carcinoma
3	not stated	Parotid gland	Non-Hodgkin B-cell lymphoma
1.5	male	Maxilla	Odontogenic carcinoma
15	male	Maxilla	Osteosarcoma
15	female	Mandible	Osteosarcoma
14	male	Maxilla	Osteosarcoma
15	male	Maxilla	Osteosarcoma
15	male	Maxilla	Osteosarcoma
12	male	Maxilla	Plasmacytoma
12	female	Palate	Plasmacytoma
6	female	Maxilla	Rhabdomyosarcoma
5	female	Lip	Rhabdomyosarcoma
9	female	Buccal mucosa	Rhabdomyosarcoma
4	male	Palate	Rhabdomyosarcoma
1	male	Lip	Rhabdomyosarcoma
11	female	Retromolar area	Rhabdomyosarcoma
7	male	Mandible	Rhabdomyosarcoma
3	female	Tongue	Rhabdomyosarcoma
12	female	Mandible	Squamous cell carcinoma
9	female	Gingiva	Squamous cell carcinoma
9	male	Tongue	Squamous cell carcinoma
10	male	Lip	Squamous cell carcinoma
7	male	Palate	Squamous cell carcinoma
13	female	Tongue	Squamous cell carcinoma

CHAPTER EIGHT

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