Dental Implications of Genetic and Congenital Intellectual Disabilities in Cape Town

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“I can’t change the direction of the wind, but I can adjust my sails to always reach my destination.”

Jimmy Dean

DECLARATION

I Tina Sharon Roberts declare that this dissertation is the result of my own work and has not been previously submitted, in part or whole, to any university or institution for any degree, diploma, or other qualification.

Signed: Signed by candidate

Date: 01.12.2018

Dedication

I dedicate this thesis to my wonderful children, Carla, Mahesh and Ashton. I am extremely grateful for your love and support.

A special feeling of gratitude to my loving parents, Cecil and Elaine Roberts whose words of inspiration and encouragement for tenacity are ever present.

To my sisters, Tracy and Hayley and their spouses, Billy and Jerome for their love and support I also dedicate this thesis to my partner Ewan Engelbrecht

And to all children with special needs

You are all

"the wind beneath my wings"

Above all to my Heavenly Father, for granting me the strength, courage and endurance throughout this study.

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I am grateful to the National Research Foundation for supporting the running costs of my PhD project via my supervisor, Prof Peter Beighton.

Abstract

Introduction

Intellectual disability (ID) is a common and significant problem which has many social, financial, medical and dental implications in South Africa. The severity of the ID varies, ranging from mild to profound impairment and numerous environmental and genetic factors play a role in the aetiology. Oral health is crucial to the overall health and well-being of children with ID. The dental problems of children with ID may be overshadowed by their intellectual dysfunction, and in some instances, by syndromic manifestations. These dental abnormalities may be unnoticed or considered of lesser importance than systemic health issues.

There is a paucity of information in both the international and local scientific literature regarding the dental needs, the dental management implications and barriers to oral care pertaining to children with ID. For these reasons, the principal focus of this thesis is the identification, documentation and analysis of the dental abnormalities a group of children with ID in Cape Town, South Africa.

Methodology

A total of 206 children with ID were assessed during the investigation; 157 children at six Special Educational Facilities (SE Facilities) and 49 at the Red Cross Children's Hospital (RXH) in Cape Town. The children were referred to the author by the Medical Genetics team of the University of Cape Town.

This clinical study was based on a cross-sectional, quantitative, exploratory, descriptive design. When appropriate, clinical photographs and panorex radiographs were obtained. Signed permission for these records were granted by the parents or legal caregivers.

Results

The frequency of unmet dental disorders among children with ID both at the SE Facilities and RXH was high: dental caries (67% and 84%); gingival disease (69% and 86%); missing teeth (46% and 51%); malocclusion (30% and 66%); structural tooth abnormalities (7.5% and 38%). Based on clinical observation, forty-three percent of children at the SE Facilities had abnormalities of the jaw and midface that required surgical intervention. Dental fillings were present in only 8% of children at the SE Facilities and 12% of children at the RXH.

Many parents and caregivers of children with ID experienced difficulty attending dental clinics. Financial and psychosocial issues were the key barriers that prevented their children from accessing dental services.

Conclusions

Intellectual disability varies in complexity and affects several South African children. Oral health plays a significant role in the general health and well-being of children with ID. The prevalence of unmet dental needs among children with ID is high, and in South Africa, the limited financial resources dedicated to primary and specialized oral health care may preclude access of many affected children to the required dental services. Furthermore, psychosocial factors such as violence, limited finance, and logistical problems such as transport may also impact on the high frequency of dental disease in this country.

The common occurrence of unmet basic and specialized dental needs reported in this study reflects the plight of children with ID in the context of dental management. The possible challenges faced by affected children in the maintenance of acceptable levels of oral health together with those encountered by oral healthcare professionals in the management of dental problems are complex yet integral to patients' quality of life. This study aims to heighten the awareness of the importance of oral health among children with ID in South Africa.

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LIST OF ABBREVIATIONS

AD: Autosomal dominant

AI: Amelogenesis Imperfecta

AAIDD: American Association on Intellectual and Developmental Disabilities

AAMR: American Association on Mental Retardation

AR: Autosomal recessive

CDC: Centre of Disease Control

CT: Cape Town

DI: Dentinogenesis imperfecta

ID: Intellectual disability

IQ: Intelligence quotient

GH: Gingival hypertrophy

RXH: Red Cross Children's Hospital

SA: South Africa

SE Facilites: Special Eductional Facilities

UCT: University of Cape Town

USA: United Sates of America

UWC: University of the Western Cape

WHO: World Health Organisation

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SECTION 1

CHAPTER 1: BACKGROUND TO THE STUDY

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Painting by: Carla Anne Roberts

CHAPTER 1: BACKGROUND TO THE STUDY

1.1 Introduction

Oral disorders can compromise an individual's quality of life. In children, they cause pain, sleep disturbances and delayed development. They also have been implicated in poor scholastic performance (Slade et al., 2005; Holt & Kraft, 2010). Inadequate dental care remains amongst the most common unfulfilled medical need in children (Benzian et al., 2011). This problem is particularly prevalent in families from low-income countries, who lack subsidised medical care and in children with special health care needs (Mouradian, 2001). Although children with ID may have similar dental problems to those without ID, they have several additional challenges including their intellectual and physical impairment, possible coexisting systemic disorders and difficulties accessing dental treatment, which can contribute to their unmet dental needs. These limitations may also prevent the affected children from performing routine oral hygiene procedures. Their dependence on a caregiver for daily oral care, their restricted ability to clear food from the oral cavity, impaired salivary flow and their preference for diets rich in carbohydrates place these children at a high risk for developing dental diseases (Norwood & Slayton, 2013). Furthermore, children with genetic ID syndromes may have additional inherent craniofacial and dental changes that increase their risks of oral disease including dental caries and gingivitis (Vigild, 1985).

The South African health care system, including dentistry, comprises of both public and private sectors. The majority of the population depend on the State to provide for their general and oral health needs. However, many health care professionals are employed in the private sector creating overcrowded State hospitals and overburdened State health workers (van Wyk & van

Wyk, 2004). The South African government has explicitly included the provision of oral health services to children with disabilities in their National Health Care Policy (Department of Health South Africa, 2003). Nevertheless, access to oral health care for children with ID is constrained by a scarcity of financial resources, lack of privately funded healthcare, the absence of adequately trained oral health personnel and long waiting lists at public hospitals.

1.2 Rationale for the study

The dental problems of children with ID may be overshadowed by their intellectual dysfunction and in some instances, by syndromic manifestations. In these circumstances their dental needs may be considered secondary and remain unnoticed.

Oral health is crucial to the overall health and well-being of children with ID. Healthy teeth and gums facilitate proper nourishment, enrich social relations, and promote self-worth.

Disorders of the oral cavity influence general health and disease. Oral bacteria can initiate infection in oral tissues particularly when the body is immunocompromised by illness or medication. Moreover, systemic conditions such as Diabetes Mellitus, which sometimes accompany genetic ID syndromes, are known to impact on the health of the oral tissue.

With this background, the present study aimed to elucidate the dental problems of children with ID and the implications of untreated dental disease. The challenges faced by children accessing dental services and those faced by the dental team managing the affected children were also assessed.

The information generated in the investigation will assist health care service deliverers to prioritize dental provision and to provide specialized dental care where necessary. It is relevant that international and local studies pertaining to the unmet dental needs of children with ID

are sparse and mainly focused on older individuals (Fernandez et al., 2015, 2016; Petrovic et al., 2016). For these reasons, the author undertook to document and discuss the dental and management implications of children with ID in Cape Town.

1.3 Aims

This investigation had the aim of identifying the unmet dental needs of children with ID attending six Special Educational Facilities (SE Facilities) in Cape Town and at the UWC-UCT Dental Genetics clinic at the Red Cross War Memorial Children's Hospital (RXH), Cape Town.

1.4 Objectives

i. To determine the prevalence rates of untreated dental caries, gingival disease, missing and filled teeth in each child using the Special Olympics Special Smiles (SOSS) evaluation tool (White, Beltran & Perlman, 2004). Malocclusion, structural tooth abnormalities as well as anomalies of the jaw and midface per participant were also documented.

ii. To compare the prevalence and percentage of specific clinical parameters amongst age groups and genders.

iii. To determine whether there was a difference in the prevalence of the clinical features at those schools that were entirely dependent on State funding and in a school that received additional funding from an external source.

iv. To describe and review dental management challenges and document possible barriers to oral health care in children with ID.

1.5 Thesis structure

Historical overview of the study

The initial intention of the study was to document the orofacial and dental changes of children with genetic ID syndromes. However, as the study progressed it was evident that there were many factors, including socioeconomic and management challenges, which faced the entire group of children with ID and the oral health professionals who treated them. For these reasons, a simple account of the dental changes among children with genetic ID syndromes would fail to place this group of children's oral health and dental needs into perspective. With this insight, the author subsequently undertook a comprehensive investigation into all possible factors that may influence their oral health.

Summary:

The project is divided into three sections and 20 chapters. During the project new developments in the field of genetics appeared in the literature and where relevant this new information was incorporated in the thesis. Tables were included in the text for the sake of accuracy. When completed, the thesis was large, with relevant references provided in the body and listed at the end of each chapter. For reasons of clarity the references were also consolidated in alphabetical order in the addendum.

There are 7 addenda at the end of the thesis. In order to obtain a comprehensive understanding of the oral health of children with ID in Cape Town, both their dental needs and management challenges were addressed during the preparation of this thesis. The dental implications of children with ID were investigated in terms of their unmet dental needs in the form of a prevalence study that took place at two different types of specialized institutions. A qualitative synopsis of the dental management implications of children with

ID is provided.

SECTION 1: BACKGROUND TO THE STUDY, LITERATURE REVIEW, METHODOLOGY AND RESULTS

The formatter comprises the title page, declaration, dedication, acknowledgments, the abstract and contents. A list of tables and figures are also included in this section. The manuscript was evaluated for plagiarism via "turnitin" software and with a score of 7%.

Chapter 1 introduces Intellectual Disability (ID) in the context of oral health and provides the rationale for the investigation and its aims and objectives.

A literature review is presented in chapter 2 and provides a historical account of the evolution, aetiology and prevalence of ID, background to institutionalization and reintegration of affected individuals into society. The dental anomalies associated with specific genetic ID syndromes are also documented. The methodology chapter (chapter 3) explains the research process. Comprehensive explanations of the research design, choice and application of data collection and the sampling aspect of the investigations are provided. The inclusion and exclusion criteria and ethical issues are also included in this chapter. Chapter 4 and chapter 5 contain the primary data collected through observations and clinical examination. The presentation of the principal data is supported by bar charts, tables and brief descriptions.

SECTION 2: DISCUSSION OF THE FINDINGS

This section is divided into 5 chapters, reports the clinical findings of the study and plays a critical role in the achievement of the research aims and objectives. The primary data are explored and discussed using comparisons with the findings published by other authors. The data relevant to each research objective are discussed separately. Clinical images, and

radiographic pictures are provided throughout this section to illustrate the observations. Tables of specific clinical features in genetic ID syndromes as observed during the study and reported in the literature are presented. The dental management implications are discussed at the conclusion of each clinical finding. Chapter 6 addresses the acquired oral diseases, namely dental caries and gingival disease, observed during the investigation. Chapter 7 focuses on abnormalities of tooth number and reviews their possible environmental and genetic causes. Changes to tooth structure are discussed in chapters 8 and 9 while changes to the midface and jaw are reviewed in chapter 10. Chapter 11 discusses the concept of malocclusion and its possible consequences in ID. This chapter also addresses changes in salivary flow and macroglossia together with their implications in children with ID.

SECTION 3: DENTAL MANAGEMENT AND SYSTEMIC CHALLENGES

This section is divided into 8 chapters. A comprehensive discussion of the dental management problems revealed by the study is provided in this section. Chapter 12 discusses the physical, psychological and behavioural challenges facing the children involved in the study. Chapter 13 gives an account of the systemic conditions that affected many children and their impact on dental management. The implications of local anaesthetics in the dental management of children with systemic involvement are also discussed in this chapter. The prevalence, clinical spectrum and the oral lesions of HIV and AIDS are discussed in chapter 14. Chapter 15 concentrates on the role of commonly used and prescribed medication in dental practice, discussing possible drug interactions and adverse effects in the dental management of children with ID. Chapter 16 reviews the selection procedure of children for dental management under general anaesthesia, the advantages and

disadvantages of this technique and the preoperative assessment of the children. Chapter 17 gives an account of the challenges faced during general anaesthesia. Chapter 18 describes various aspects of conscious sedation in the dental management of children with ID. Chapter 19 discusses various social issues that may present barriers to oral health care in children with ID, based on conversations between the author and the children's parents or caregivers.

Chapter 20, concludes the investigation and contains a summary of findings and the author's recommendations with respect to possible improvements on intervention strategies for the prevention oral diseases of children with ID in South Africa.

References:

1. Benzian, H., Monse, B., Heinrich-Weltzien, R., Hobdell, M., Mulder, J., van Palenstein Helderman, W. 2011. Untreated severe dental decay: a neglected determinant of low body mass index in 12-year-old Filipino children. *BMC Public Health*. 11(1):558. doi: 10.1186/1471-2458-11-558.
2. Department of Health South Africa. 2003. *National Policy for Oral Health in South Africa*. Available: https://www.westerncape.gov.za/text/2003/national_policy_oral_health_sa.pdf
3. Fernandez, C., Declerck, D., Dedecker, M., Marks, L. 2015. Treatment needs and impact of oral health screening of athletes with intellectual disability in Belgium. *BMC Oral Health*. 15(1):170. doi: 10.1186/s12903-015-0157-9.
4. Fernandez, C., Descamps, I., Fabjanska, K., Kaschke, I., Marks, L. 2016. Treatment needs and predictive capacity of explanatory variables of oral disease in young athletes with an intellectual disability in Europe and Eurasia. *European Journal of Paediatric Dentistry.* 17(1):9–16.
5. Holt, K. & Kraft, K. 2010. Oral health and learning. *Journal of the Oklahoma Dental Association*. 97(1):24–25.
6. Mouradian, W.E. 2001. The face of a child: children's oral health and dental education. *Journal of Dental Education*. 65(9):821–831. doi: 10.1177/001789690106000411.
7. Norwood, K.W. & Slayton, R.L. 2013. Oral health care for children with developmental disabilities. *American Academy of Pediatrics*. 131(3):614–619. doi: 10.1542/peds.2012-3650.
8. Petrovic, B.B., Peric, T.O., Markovic, D.L.J., Bajkin, B.B., Petrovic, D., Blagojevic, D.B., Vujkov, S. 2016. Unmet oral health needs among persons with intellectual disability. *Research in Developmental Disabilities*. 59:370–377. doi: 10.1016/j.ridd.2016.09.020.
9. Slade, G.D., Nuttall, N., Sanders, A.E., Steele, J.G., Allen, P.F., Lahti, S. 2005. Impacts of oral disorders in the United Kingdom and Australia. *British Dental Journal*. 198(8):489–493. doi: 10.1038/sj.bdj.4812252.
10. van Wyk, P. & van Wyk, C. 2004. Oral health in South Africa. *International Dental Journal*. 54:373–377.
11. Vigild, M. 1985. Prevalence of malocclusion in mentally retarded young adults. *Community Dentistry and Oral Epidemiology*. 13(3):183–184. doi: 10.1111/j.1600-0528. 1985.tb00441. x.
12. White, J.A. & Beltran, E.D. & Perlman, S., 2004. Training Manual for Standardized Oral Health Screening Training Manual for Standardized Oral Health Screening. Availble: http://media.specialolympics.org/resources/health/disciplines/specialsmiles/Special-Smiles-Training-Manual.pdf.

CHAPTER 2: LITERATURE REVIEW-INTELLECTUAL DISABILITY

Introduction

In order to provide an appropriate background, the historical evolution of concepts and terminology pertaining to ID is the central theme of this chapter.

2.1 The evolution of the understanding of Intellectual Disability (ID)

The history of ID is interwoven with that of social, political, religious and cultural development. Differences between understandings of its cause are dependent upon individual perceptions of the disorder and the nomenclature applied to ID has been correspondingly variable.

The first known reference to ID appeared in the Egyptian Papyrus of Thebes in the early 16th century BC (Sheerenberger, 1983).

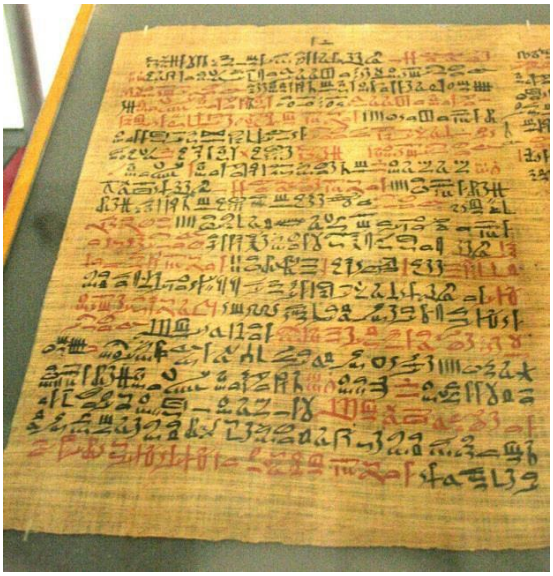


Fig 2.1 Egyptian Papyrus of Thebes

Google: https://www.thinglink.com/scene/800343759001747458

In the late fifth century BC, Hippocrates alluded to ID as being a result of imbalances in the four humours in the brain while the ancient Romans and Greeks believed ID to be a form of spiritual punishment by the gods (Harris, 2006). In the West, the notion of mystical aetiologies persisted into the 15th century AD when disabilities were attributed to witchcraft and demonic forces. The Maleus Maleficarum, published in 1487 for the Inquisition, suggested that fairies and demons caused babies to be born with ID as punishment for their parents' evil doing or for those who were led astray by demonic spirits. The infants of these parents were therefore deemed to be possessed by an evil force (Nyland, 2002).

During the Middle Ages, physicians began categorizing ID according to competency in mathematics and social skills. Descriptive terms such as "idiot," "fool," "non-compos mentis," or "innocents" emerged. The lack of social skills was associated with the individual's inability to perform tasks such as counting to 20, identifying family members and performing daily routines unaided. Such persons were in general harmless to society. However, "lunatics" posed a danger to themselves and others and lunacy was considered to be a temporary condition linked to the moon. The "idiots" were recognized as "incurably and naturally damaged" (Rushton, 1988).

Montalto, in Florence in 1614, published the first documented "classification" of ID from a clinical perspective (Bay and Lipkin, 2011). This physician, who took a keen interest in ID, distinguished it from other neurological disorders and suggested that these conditions originated in the brain. He also proposed that ID might be the result of birth defects, damage to the brain during birth and postnatal causes. Thomas Willis, a seventeenth-century physician who coined the term "neurology", was the first person to refer to ID as a "disease".

He believed that alterations in brain function occurred as a result of structural abnormalities in the brain; these being either congenital or acquired (Williams, 2002).

Fig 2.2 Thomas Willis 1621-1675

Google: http://www.thefamouspeople.com/profiles/thomas-willis-6428.php

In 1846 Samuel Howe, a reformist in the education of physically disabled persons, suggested that ID may be the result of unhealthy lifestyles, consanguineous marriages, heredity, greed and excessive or deviant sexual activity. This renowned educationalist also alluded to a heritable aetiology of ID (Reynalds, Zupanick & Dombeck, 2015). In 1866 a British physician John Langdon Down suggested that physical features may assist in recognition of specific ID conditions (Frydman & Nowzari, 2012). In this way, the well-known Down syndrome came to be delineated.

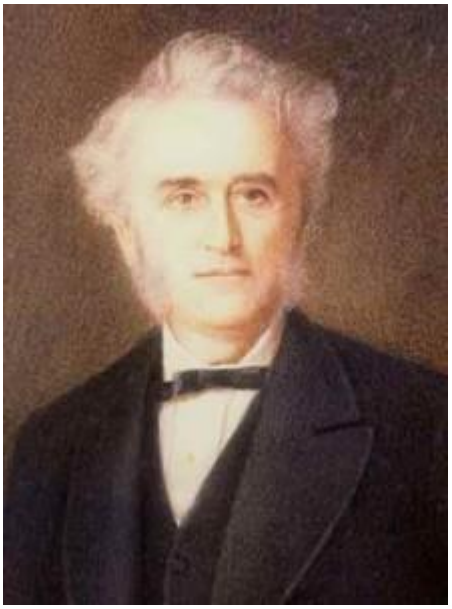


Fig 2.3 John Langdon Down 1828-1896

Google: http://miriam-may.com/wp-content/uploads/imgDown-222x300.jpg

In 1882 William Ireland, regarded as a pioneer in defining the aetiology of ID, noted the following findings regarding ID (Ireland 1882):

1. May be inherited
2. Is common in individual families
3. Could be caused by conditions such as epilepsy
4. Certain illnesses could result in ID
5. Could accompany seizures

Ireland also correlated several physical characteristics with particular causes of ID. These included an unusually small head, palatal and dental abnormalities. Furthermore, he differentiated profoundly impaired individuals ("Fools") from less impaired persons ("Idiots"). While Idiots had a fair amount of muscular control and cognitive functioning, Fools had

intellectual deficiencies and major speech impediments. Later, the classification was expanded to include “Simpletons”. These individuals possessed motor skills and sufficient cognitive abilities to complete daily activities with minimal assistance but lacked social skills.

Other historical terms used to describe ID include “Cretin”, “Ament” and “Retarded”. These were initially medical terms intended to identify the cause of ID. However, as they entered the vernacular, they acquired a stigmatizing connotation and presently have little contemporary medical significance (Reynalds, Zupanick & Dombeck, 2015).

Between the late 19th and early 20th centuries, the detection and evaluation of ID was required for educational purposes and formal assessment of individuals. In 1961 the term “Mental Retardation” was adopted by the American Association on Mental Retardation (AAMR), presently known as the American Association on Intellectual and Developmental Disabilities (AAIDD). This term replaced designations such as “feeblemindedness” and “ideosity” which were regarded as derogatory. As time passed, ID became increasingly recognised as a brain condition with medical causes. Nevertheless, until the late 20th century these terms were used for the categorization of persons living in special institutions for the intellectually impaired. In this way, appropriate levels of care could be provided.

Although the familial nature of some forms of ID has long been recognized, the concept of specific heritable causes of ID is relatively recent.

2.2 Current concepts and definition of ID

Intellectual disability is currently defined as “a disability characterized by significant limitations, both in intellectual functioning and in adaptive behavior as expressed in conceptual, social, and practical adaptive skills. This disability originates before the age of 18 years” (AAIDD, 2013).

"A significant limitation in intellectual functioning" refers to a limited aptitude to perform tasks such as problem-solving, the ability to reason and understand. An intelligence quotient (IQ) test is a determinant of intellectual functioning and an IQ test score of less than 75 may indicate a restricted intellect.

"Adaptive skills" refers to an age-appropriate activity that allows individuals to function independently and includes their social, conceptual and practical abilities. When determining the level of adaptive behaviour of an individual, environmental factors such as cultural and language diversity, social and economic conditions also require consideration (AAIDD, 2013). In 2008, Whitaker expressed a concern that the current definition of ID through both IQ and adaptive behaviour is difficult to assess accurately. He argued that the ability to cope, that is, adaptive behaviour, is often independent of IQ (Whitaker, 2008).

In 2012, the World Health Organisation (WHO) assigned the AAIDD to review the terminology, diagnostic criteria, classification, and the testing of ID to be used in the 'International Classification of Diseases' of the 11th revision (ICD-11). The amendment was due for completion in 2015 and implementation in 2018. The suggested changes to the terminology include: the name of ID to be replaced by "disorder of intellectual disability" and its definition changed to "disorder of intellectual disability is a condition characterized by significant limitations in intellectual functioning and adaptive behaviour, originating during the developmental period". Further suggestions include the simplification of the diagnostic guidelines of ID and that the term "learning" should be removed from the diagnostic criteria. Previous categories of "mild", "moderate", "severe" and "profound" to be changed to "Disorder of Intellectual Disability, marked, extensive, pervasive and other" (Tassé, Luckasson & Nygren, 2013)

2.3 Prevalence of ID

The measured prevalence of ID differs between studies from different countries (Maulik et al., 2011). Factors influencing prevalence data include the age at which a diagnosis is made, the possible use of inconsistent diagnostic criteria and the source of statistical data (Roeleveld and Zielhuis, 2008). In some instances, ID may be diagnosed on the presence of delayed developmental milestones or when learning difficulties present themselves at school. Other times, ID is based exclusively on the IQ or cognitive behaviour of an individual.

Prevalence data for ID for some regions African regions are available from the literature: Mozambique 1.9% rural versus 1.3% urban (Patel et al., 2007) and Ethiopia 10.3% (Fitaw & Boersma, 2006).

In South Africa there is a lack of published literature on ID (Adnams, 2010). In 1999, following the first National Disability Survey, the prevalence of ID in South Africa was reported to be 1.1% (Schneider et al., 1999). In 2005, Statistics South Africa circulated the findings of a national census survey conducted in 2001, indicating the population prevalence of ID to be 0.5% (Statistics South Africa, 2005). In this analysis, persons with ID residing in special care facilities were excluded thus influencing the accuracy of the data. An additional national survey focusing solely on severe ID reported the population prevalence to be 0.27% (Statistics South Africa, 2007). Two smaller studies performed by trained staff using standardized questionnaires yielded prevalence rates for mild ID of 1.7% and 2.9% respectively (Couper J, 2002; Kromberg et al., 2008).

The most recent published prevalence rates for mild ID is 4.2 % and for severe ID 1% (Statistics South Africa, 2014). These figures may have been prejudiced by the migration of people into Sub-Saharan Africa and South Africa after 2004. However, a single study from the Western

Cape reported the frequency of ID amongst both adults and children to range between 0.1% (severe ID) and 2.5% (mild ID) (Kleintjes et al., 2006). These figures may have changed as a result of changing demographics in the Cape Province. None of the South African studies mentioned what the diagnostic criteria was used to identify ID. The prevalence of ID in many African countries is influenced by factors such as the scarcity of trained diagnosticians and the lack of resources for analysis (Njenga, 2009). The absence of a centralized database for recording ID conditions in South Africa has resulted in a lack of such critical information and data pertaining to its aetiology. Nevertheless, scanty information obtained from State-funded health care facilities suggests that the causes of ID in South Africa are comparable to those in high-income countries (Adnams, 2010).

2.4 Aetiology and diagnostic challenges of ID

The general causes of ID are summarized in Table II.1 and are broadly classified as either genetic or environmental. However, the aetiology of a large proportion of cases remains unknown. Specific diagnoses of ID syndromes may be difficult to establish in the absence of obvious clinical signs and a positive family history. In addition, genetic causes of ID in the African context are difficult to establish due to extensive genetic variation and the general paucity of genetic and genomic research on African populations. Furthermore, several genetic tests are based on European gene panels and may not be relevant to affected individuals of African ancestry.

Table II.1: The broad classification of the aetiology of ID

Prenatal	**Developmental (Multifactorial)**
	Chromosomal
	Genetic
	Embryopathic
	Infective
Perinatal	Acquired Mental Handicap a. Cerebral Palsy b. Birth trauma c. Anoxia d. Kernicterus e. Infection
Infancy and Childhood	a. Inherited b. Metabolic disorders c. Trauma

In a study of a rural South African population, the origin of ID remained unknown in 73% of affected individuals, congenital factors were identified in 21% and 6 % were attributed to environmental influences (Christianson et al., 2002). The study, however did not specify whether the congenital influences were heritable in nature, neither did it specify the participant's level of ID.

Mild forms of ID in individuals with IQs between 50 and 70 are most common and constitute between 80-85% of all intellectual disabilities. In most instances, this condition arises from an interaction between genetic and environmental factors. Unfortunately, there has been little advance in identifying the genetic aspects predisposing individuals to the development of mild ID. An important obstacle in this area of research is the challenge to recognize normal and mildly affected family members (Ropers, 2010). General risk factors associated with ID in

high-income countries such as the United States of America include low birth weight, prenatal and perinatal difficulties (Seidman et al., 2000; Boulet, Schieve & Boyle, 2011).

Moderate to severe forms of ID (IQ < 50) are usually easily recognizable, are often associated with additional neurological or systemic features and constitute 15% of all ID. Chromosomal and genetic abnormalities cause 30% to 40% of moderate-to-severe ID (Flint, 2001). Several pathological pathways have been implicated in genetic ID syndromes and with advancing technology it is possible that additional mechanisms will be elucidated. Globally, Down syndrome (DS) remains the most common chromosomal form of ID. The prevalence of DS in South Africa varies across ethnic, age and sociodemographic groups, but its overall rate is reported as between 0.7 and 1.5 per 1000 children (Molteno et al., 1997; Christianson et al., 2002). These figures may have changed in view of a decrease in the utilization of amniocentesis and limited genetic counselling services at specialized health care facilities in South Africa (Urban et al., 2011).

Although Emerson (2004) reported a significant association between poverty and ID in high-income countries, the relationship between poverty and ID in South Africa has yet to be clarified. Other environmental factors assumed to contribute to the initiation and development of ID in this country include nutritional deficiencies, transmissible diseases including HIV/AIDS and tuberculous meningitis, foetal alcohol spectrum disorder as well as violence and injury (Adnams, 2010).

Malnutrition during the developmental period of life is related to longstanding shortfalls in perception, performance and physical abilities. In turn, these may be exacerbated by socioeconomic influences (Grantham-McGregor & Baker-Henningham, 2005). Grantham-McGregor et al. (2007) verified these findings in a group of malnourished South African

children entering primary school who demonstrated poor academic performance and impaired perceptual skills

In a systematic review of the effects of HIV on intellectual functioning, Sherr, Mueller & Varrall (2009) reported that infection with the Human Immunodeficiency Virus had been found to be harmful to cognitive development in 81% of studies worldwide. These findings were corroborated in a similar review from countries in Sub-Saharan Africa by Banks et al. (2015).

The frequency of tuberculosis (TB) in the Western Cape is high (van Well et al., 2009). Meningitis, a complication of pulmonary TB is associated with a high level of morbidity and mortality especially among children, who may develop life-threatening neurological complications. HIV co-infection increases the risk of developing TB associated meningitis and its complications, the most important in South African children being moderate to severe ID.

Foetal alcohol spectrum disorder (FASD) is a disorder that "includes a range of permanent conditions that result from alcohol exposure of the fetus in utero. Foetal Alcohol Syndrome (FAS) is the most severe condition in this spectrum" (Rendall-Mkosi, et al., 2008). Persons affected by FASD normally suffer from mild to moderate ID. The global prevalence rates of FASD varies between countries: in European countries such as Croatia and Poland the frequency of FASD and related disorders ranges between 2 and 6% (Petković & Barišić, 2013). In some regions of the United States of America recent studies have reported a frequency of between 3% and 8% among young children (Centres of Disease Control, 2015). The prevalence of FASD in rural areas of South Africa is reported to be the highest in the world (20-28%) amongst children of similar age (May et al., 2017).

Violence and injury result in significant rates of morbidity and mortality in South Africa. In particular, traumatic brain injury is an important cause of ID among children and adults in this country.

2.5 Rehabilitation and intervention of persons with ID

Since ancient times persons with physical or neurological impairments or behavioural problems have been devalued and marginalized within society. They have often been perceived as “subhuman,” a “menace,” and a “burden” (Shereenberger, 1983).

In the late 17th century the English philosopher and physician John Locke suggested that the environment influenced certain physical and emotional traits. He held that thoughts, beliefs, and personality were not inherent but rather were learned (Reynalds, Zupanick & Dombeck, 2015). This view transformed the understanding of ID and became the cornerstone of psychotherapy and rehabilitation.

Both social and medical interest in ID resulted in a considerable increase in the number of persons with ID being institutionalized during the 1800s. In the mid-19th century, Edouard Sequin, a physician and student of John Locke, formulated special techniques to educate children with ID using the five senses. In 1876 he became the first president of the “Association of Medical Officers of the American Institutions for Idiotic and Feebleminded Persons” (now known as the AAIID), the world's oldest and largest inter-disciplinary professional organization for intellectual disabilities.

Fig 2.4 Bethlehem Royal Hospital, the first British mental asylum – founded in 1247

Google: http://i-fakt.ru/chto-znachit-bedlam/

As social attitudes changed and stigmatization amplified in the late 19th century, the trend to admit children with ID to special care facilities increased in Europe and North America.

These facilities lacked both medical and educational resources and mainly served to isolate affected individuals. The idea of institutionalization evolved into a dichotomy. On the one hand it protected some persons from neglect leading to illness and death. On the other hand, the institutions were themselves places of abuse and mistreatment of vulnerable individuals. Nevertheless, it was in these “places of safety” that the medical aetiology of ID and mental illness gradually emerged.

Facilities in South Africa

In South Africa affected individuals initially were placed in general hospitals. In Cape Town, however, overcrowding forced the State to transfer some patients to Robben Island to live among prisoners and lepers.

Fig 2.5 Robben Island prison

Google: https://www.thesouthafrican.com/nelson-mandelas-living-legacy-lonely-years-on-the-island/

In 1891 the first patients were transferred from Robben Island to the specially built Valkenberg Asylum in Maitland, Cape Town (Western Cape Government, 2006). In 1921 the Alexandra Institution, the first South African rehabilitation facility for persons with ID, was officially opened in Cape Town. Suitable patients were transferred from Valkenberg Asylum and hospitals in the area. At first only females were admitted but later men also became patients. A school for the education and rehabilitation of children was established on the premises. Instructions in crafts such as needlework were also provided for older children (Minde 1975).

Fig 2.6 Valkenberg Hospital

Google https://www.iol.co.za/capetimes/news/valkenberg-hospital-gets-a-makeover-2092850

In Gauteng, the Witrand Institution in Potchefstroom, initially used as a military base for British troops, was converted into an institution for persons with ID in 1923. This facility had well equipped educational and medical resources and catered for both children and adults.

Umgeni Waterfalls Institution, in KwazuluNatal, was opened in 1949 and the first patients were transferred from the Witrand Institution. Like its predecessors, this facility was well managed with training, recreational and medical facilities.

Before the dissolution of apartheid in South Africa, facilities for people with ID were generally only available to those classified as “White”. However, in 1962 after almost 50 years motivation, the Westlake facility in Cape Town was opened for the “Coloured” population by the National Council of Mental Health.

The history of specialized education for “Black” South African children wih ID remains obscure. The reasons for this includes neglect in the apartheid era and the traditional belief systems existing in this population group. The integration of the school systems across ethnic groups after 1994 provided admission for all South African children to special care facilities.

From the early 1900s several private facilities for people with ID were developed in major South African cities. The financing of these establishments is from the parents, voluntary organizations and the State. It is relevant that these facilities are accredited and controlled by the Government.

2.6 De - institutionalization

The concept of de-institutionalizing persons with ID was initiated in Scandinavia during the 1960s and formalized in the 1970s (Nirje, 1994). Although the model was based on the concept of community integration, several additional reasons prompted the restructuring of care for persons with ID, including overcrowding and decreased funding for asylums.

Strategies for rehabilitation in the community were formally introduced in several countries during the late 1960s and early 1970s. Ever since then the number of institutionalized people with ID has been decreasing in England (Mansell, 2006) and the United States of America (Braddock, Hemp & Rizzolo, 2004; Coucouvanis et al., 2006). In some other countries notably Norway and Sweden, institutions for persons with ID no longer exist (Braddock et al., 2001; Beadle-Brown, Mansell & Komza, 2007).

Globally, the inclusion of persons with ID into their communities has encountered several obstacles. In some countries the process has taken place over several years in order to assist individuals to attain the maximum degree of independence. Nevertheless, the sudden closure of specialized facilities has challenged all aspects of inmates' lives as well as those of their families and communities.

In South Africa after 1997, large numbers of persons with ID were reintegrated into their communities.

Fig 2.7 Children with ID after competing in an indoor rock climbing event. They are fully integrated into their communities. The boy on the left is affected by Coffin-Lowry syndrome and the one on the right has ID of unknown aetiology. The young girl holding a T-shirt is unaffected.

In the light of new developments in human rights and governmental restructuring, the management of mental health needs was transferred to the primary health care sector (Petersen et al., 2009). There is still a perceived lack and inefficient use of resources for mental health care within this sphere, which provides only for emergency and chronic mental health issues. The tragic loss of life in 2017 at several South African special health care facilities for persons with ID resulting from pneumonia, dehydration, malnutrition and diarrhoea, highlights the plight of such persons in this country.

2.7 The unmet dental needs of children with ID

Good oral health is imperative for mastication, aesthetics, communication and quality of life; however, it is often inadequate in children with ID (Morgan et al., 2012; Gomes et al., 2014). Furthermore, the frequency of both preventable oral diseases such as dental caries and periodontal disease (Petrovic et al., 2016; Diab et al., 2017) and of more complex oral disorders such as malocclusion (Cabrita, Bizarra & Graça, 2017) remains high and is a reflection of the unmet dental needs of these children.

The unmet dental needs in children with ID may originate from their own inability to attain proper oral hygiene or to express pain and discomfort to their immediate environment. Moreover, the failure of relatives or caregivers to assess the children's oral health could result in an increase in the dental diseases burden among these children. Socioeconomic influences such as the absence of financial resources both personal and within the health sector, the paucity of services and a deficiency of knowledgeable professionals willing to treat children with ID, may all contribute toward the high frequency of dental needs among these children.

2.7.1 Dental Caries and periodontal disease in ID

The environmental aetiological agents resulting in the initiation and progression of both dental caries and periodontal disease are well-known. The interactions between dental plaque, cariogenic bacteria, and a sucrose-rich diet will over time result in the formation of an early carious lesion. Likewise, specific pathogens have been implicated in the aetiology of periodontal disease. A common dietary risk factor for both diseases is the fermentable group of carbohydrates namely sucrose. In dental caries, oral microbes ferment sucrose resulting in the production of the lactic acid which over time initiates the demineralization of enamel.

In periodontitis, glycaemia initiates and stimulates oxidative processes and in advanced glycation the final products may trigger a hyper inflammatory state. Similarly, hyperglycemia may inhibit the proliferation of the periodontal ligament and prevent its differentiation into osteoclasts in vitro (Malvania et al., 2016).

The risk, prevalence and severity of dental caries and gingival disease (periodontal disease) may be influenced by the oral microbiome. Disturbances in the oral flora may result in systemic disease including cardiovascular conditions or could aggravate existing conditions including Diabetes Mellitus. Children with ID and a concomitant compromised systemic health could therefore be prone to develop more oral disease.

Micronutrient deficiencies, such as for vitamin C, vitamin D or vitamin B12, may be related to the onset and progression of both dental caries and gingivitis (Hujoel & Lingström, 2017). Additional causative factors for these conditions include impaired salivary flow, certain autoimmune disorders such as rheumatoid arthritis (Kaur, White & Bartold, 2012) and undiagnosed or poorly controlled diabetes mellitus.

There is a paucity of evidence associating genetic factors with either the initiation or development of periodontal diseases (Slayton, 2006) and dental caries (Opal et al., 2015). The genes possibly linked with a high caries risk include: *Tuftelin* (Slayton, Cooper & Marazita, 2005), *MPPED2 and ACTN2* (Stanley et al., 2014) and *MMP10*, *MMP14, and MMP16* (Lewis et al., 2017).

Genes implicated in chronic periodontitis include those controlling bone remodelling such as *vitamin D receptor* (*VDR*) and inflammatory modulators such as *Fc gamma receptor IIA (Fc-γRIIA)* and *Interleukin 10 (IL10)* genes (Chapple et al., 2017).

Genes determining the characteristics of saliva (*AQP5*) and immune regulatory genes could play a potential role in both diseases. Mutations in *rs7791001* in *7q22.3* (Nibali et al., 2017) whose function currently remains unknown, have also been implicated as potential risks for both dental caries and periodontitis. It is also relevant that no common genetic link between dental caries and periodontal disease has yet to be established. Neither has a positive genetic link between these two disorders and ID has been elucidated.

Globally, the prevalence of both dental caries and gingival disease is high in persons with ID (Trihandini et al., 2013; Gardens et al., 2013; Nemutandani, Adedoja & Nevhuhlwi, 2013; Abijeth, Kumar & Durgha, 2015; Fernandez et al., 2015). Although both conditions are preventable, they have a multifactorial aetiology, especially in children with ID.

2.7.2 Missing teeth

The absence of teeth disrupts the relationship between the dentition and the jaw bone. There is a lack of stimulation of the oral structures resulting in bone and gingival resorption. Other consequences include anterior drifting of the remaining teeth into the vacant space, overeruption of opposing teeth into the space previously occupied by an extracted tooth, malocclusion and temporomandibular joint dysfunction. Non-dental consequences include poor aesthetics, reduced function and a low self-esteem.

Common causes of missing teeth include dental extractions, periodontal disease and physiological exfoliation. In rare instances, there may be a failure of one or more teeth to erupt into the oral cavity. The term “hypodontia” refers to the congenital absence of teeth while “anodontia” implies a congenital absence of all teeth. Both phenomena have a broad aetiological spectrum and may involve both environmental and genetic factors. Several environmental factors such as infections, toxins and radio- or chemotherapy are common

causes of missing permanent teeth (Al-Ani et al., 2017). Equally, several dominant, recessive and X-linked genetic forms of hypodontia are not uncommon. Hypodontia is also frequently associated with inherited ID syndromes including the Kabuki and Williams syndromes.

2.7.3 Malocclusion

The expression "occlusion" refers to the manner in which the maxillary and mandibular teeth come into contact. This phenomenon depends on the relationship of the upper and lower jaws and the relationship of individual teeth to each other. "Malocclusion" refers to inappropriate tooth contact. This anomaly has a variable aetiology that includes both environmental factors such as thumb sucking and genetic influences, of which some may cause severe cranial anomalies. Structural variations in the cranium sometimes accompany genetic ID syndromes. Malocclusion in children with ID, is frequently the result of musculoskeletal anomalies, changes in the cranial-base relationships, premature eruption of teeth, post-surgical complications, and incompetent lips. (Winter, Baccaglini & Tomar, 2008; Cabrita, Bizarra & Graça, 2017).

As with its aetiology, the consequences of "malocclusion" are variable and dependant on its severity. The management of malocclusion requires specialized intervention and it may involve a multidisciplinary team including surgeons, orthodontists and periodontists. In the South African context, this intervention is considered costly and at tertiary State-funded institutions may result in several years on hospital waiting lists. Additional factors which necessitate consideration in the management of children with malocclusion includes patient compliance and tolerance of orthodontic appliances. These factors may influence the treatment protocols for malocclusion among children with ID. In instances where

uncontrolled gag reflexes or inappropriate behaviour accompanies the disorder, orthodontic management may be contraindicated.

2.7.4 Structural tooth abnormalities

Abnormalities in tooth structure may cause aesthetic, functional and psychological concerns among children with ID. Defective enamel and/or dentine and misplaced teeth may also result in a higher risk of dental caries, periodontal disease and malocclusion. As with missing teeth and malocclusion, structural tooth abnormalities have both a variable aetiology and outcome.

2.8 Dental management considerations for children with ID

The general dental management of children with ID is no different to that for non-ID children. However, providing the former with optimal oral care may require the adaptation of dental expertise and approaches to delivering treatment. Furthermore, children with ID may have coexisting systemic conditions requiring special attention before or during dental procedures,such as diabetes mellitus, epilepsy, cardiovascular and respiratory problems. Hypersensitivity to drugs and drug interactions are also important in this group of children. Additional challenges which can influence the practical aspects of dental management include short stature, visual and hearing impairment and difficulty in communicating. Behavioural problems, whether due to anxiety or prior negative dental experiences, are common among children with ID and these may necessitate either conscious sedation or general anaesthesia. These techniques, although effective in delivering the desired environment for dental management, also necessitate special consideration especially in children with coexisting systemic challenges. Finally, social and financial aspects such as violence and access to oral health care may impact on the high frequency of oral disease among children with ID.

Concluding comments:

This chapter contained a comprehensive overview of the historical evolution of ID, the global and local prevalence and the dental needs of children with ID. Although persons with ID have been marginalized throughout history, continual efforts have been made to reintegrate them into society. Care has been taken by health care professionals and members of society to remove the stigma attached to this disorder and insights into the aetiology have been made. However, the dental health of many affected individuals may have been neglected or overshadowed by factors relating to their general health or their psychosocial milieu.

References

1. AAIDD. 2013. *Definition of Intellectual Disability*. Available: http://aaidd.org/intellectual-disability/definition#.Vo-U6vl96zc.
2. Abijeth, B., Kumar, S. & Durgha, K. 2015. Dental anomalies and oral hygiene status in mentally retarded children. *Asian Journal of Pharmaceutical and Clinical Research*. 8(5):195–198.
3. Adnams, C.M. 2010. Perspectives of intellectual disability in South Africa: epidemiology, policy, services for children and adults. *Current Opinion in Psychiatry*. 23(5):436–440. doi: 10.1097/yco.0b013e32833cfc2d.
4. Al-Ani, A., Antoun, J., Thomson, W., Merriman, T. & Farella, M. 2017. Hypodontia: An update on its etiology, classification, and clinical management. *BioMed Research International*, 2017:1-9.
5. Banks, L.M., Zuurmond, M., Ferrand, R., Kuper, H. 2015. The relationship between HIV and prevalence of disabilities in Sub-saharan Africa: systematic review. *Tropical Medicine and International Health*. 20(4):411–429. doi:10.1111/tmi.12449.
6. Bay, M & Lipkin, P.2011. Intellectual Disability: historical note and nomenclature. Available at: http://www.medmerits.com/index.php/article/intellectual_disability/P1. [Accessed: 2016-01-19]
7. Beadle-Brown, J., Mansell, J. &, Komza, A. 2007. Deinstitutionalization in intellectual disabilities. *Current Opinions in Psychiatry*. 20(5):437–442. doi:10.1097/YCO.0b013e32827b14ab.
8. Boulet, S.L., Schieve, L.A. & Boyle, C.A. 2011. Birth weight and health and developmental outcomes in us children, 1997-2005. *Maternal and Child Health Journal*. 15(7):836–844. doi:10.1007/s10995-009-0538-2.
9. Braddock, D., Emerson, E., Felce, D., Stancliffe, R.J. 2001. Living circumstances of children and adults with mental retardation or developmental disabilities in the United States, Canada, England, Wales, and Australia. *Mental Retardation and Developmental Disabilities Research Reviews*. 7(2):115–121. doi:10.1002/mrdd.1016.
10. Braddock, D., Hemp, R. & Rizzolo, M. 2004. State of the States in developmental disabilities: 2004. *Mental Retardation.* 42(5):357–370.
11. Cabrita, J.P., Bizarra, M. & Graça, S.R. 2017. Prevalence of malocclusion in individuals with and without intellectual disability: a comparative study. *Special Care in Dentistry*. 37(4):181–186. doi:10.1111/scd.12224.

12. Centres for Disease Control and Prevention.2015. Fetal Alcohol Syndrome among children aged 7–9 Years — Arizona, Colorado, and New York, 2010.*Morbidity and Mortality Weekly Report.* 64(03):54-57. [Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6403a2.htm?s_cid=mm6403a2_w]

13. Chapple, I.L.C., Bouchard, P., Cagetti, M.G., Campus, G., Carra, M.C., Cocco, F., Nibali, L., Hujoel, P. & et al. 2017. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint efp/orca workshop on the boundaries between caries and periodontal diseases. *Journal of Clinical Periodontology*. 44(Suppl 18):39–51. doi:10.1111/jcpe.12685.

14. Christianson, A.L., Zwane, M.E., Manga, P., Rosen, E., Venter, A., Downs, D., Kromberg, J.G.R. 2002. Children with intellectual disability in rural South Africa: prevalence and associated disability. *Journal of Intellectual Disability Research* .46(Pt 2):179–186.

15. Coucouvanis, K., Lakin, K.C., Prouty, R., Webster, A. 2006. Reductions continue in average daily populations of large state facilities; nearly 70% decrease between 1980 and 2005. *Mental Retardation*. 44(3):235–238.

16. Couper, J. 2002. Prevalence of childhood disability in rural Kwazulu-Natal. *South African Medical Journal*. 92:549–552. doi:10.1093/annonc/mdt428.

17. Diab, H.A., Salameh, Z., Hamadeh, G.N., Younes, G. & Ayoub, F. 2017. Oral health status of institutionalized individuals with intellectual disabilities in Lebanon. *Journal of Oral & Maxillofacial Research*. 8(1): e4. doi:10.5037/jomr.2017.8104.

18. Emerson, E. 2004. Poverty and children with intellectual disabilities in the world's richer countries. *Journal of Intellectual & Developmental Disability*. 29 (4):319-338. doi:10.1080/13668250400014491

19. Fernandez, C., Declerck, D., Dedecker, M.&Marks, L. 2015. Treatment needs and impact of oral health screening of athletes with intellectual disability in Belgium. *BMC Oral Health*. 15:170. doi:10.1186/s12903-015-0157-9.

20. Fitaw, Y. & Boersma, J.M.F. 2006. Prevalence and impact of disability in north-western Ethiopia. *Disability and Rehabilitation*. 28(15):949–953. doi:10.1080/09638280500404552.

21. Flint, J. 2001. Genetic basis of cognitive disability. *Dialogues in Clinical Neuroscience*. 3(1):37–46.

22. Frydman, A. & Nowzari, H. 2012. Down syndrome-associated periodontitis: a critical review of the literature. *Compendium of Continuing Education in Dentistry*. 33(5):356–361.

23. Gardens, S.J., Krishna, M., Vellappally, S., Alzoman, H., Halawany, H.S., Abraham, N.B.&Jacob, V. 2013. Oral health survey of 6-12-year-old children with disabilities attending special schools in Chennai, India. *International Journal of Paediatric Dentistry*. 24(6):424–433. doi:10.1111/ipd.12088.

24. Gomes, M.C., Pinto-Sarmento, T.C., Costa, E.M.M., Martins, C.C., Granville-Garcia, A.F., Paiva, S.M. 2014. Impact of oral health conditions on the quality of life of preschool children and their families: a cross-sectional study. *Health and Quality of Life Outcomes*. 12:55. doi:10.1186/1477-7525-12-55.

25. Grantham-McGregor, S. & Baker-Henningham, H. 2005. Review of the evidence linking protein and energy to mental development. *Public Health Nutrition*. 8(7A):1191–1201.

26. Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L., Strupp, B.2007. Developmental potential in the first 5 years for children in developing countries. *Lancet.* 369(9555):60-70. doi: 10.1016/S0140-6736(07)60032-4

27. Harris, J. 2006. Intellectual disability: understanding its development, causes, classification, evaluation and treatment. *Oxfort University Press*.

28. Hujoel, P.P. & Lingström, P. 2017. Nutrition, dental caries and periodontal disease: a narrative review. *Journal of Clinical Periodontology*. 44 (Suppl 18):79–84. doi:10.1111/jcpe.12672.

29. Ireland, W. 1882. On the diagnosis and prognosis of idiocy. *Edinburgh Medical Journal*. 1072–1085.

30. Kaur, S., White, S. & Bartold, M. 2012. Periodontal disease as a risk factor for rheumatoid arthritis: a systematic review. *JBI Database of Systematic Reviews and Implementation Reports*. 10(42. Suppl):1–12. doi:10.11124/jbisrir-2012-288.

31. Kleintjes, S., Flisher, A.J., Fick, M., Railoun, A., Lund, C., Molteno, C. & Robertson, B.A. 2006. The prevalence of mental disorders among children, adolescents and adults in the Western Cape, South Africa. *South African Psychiatry Review*. 9:157–160. doi:10.4314/ajpsy. v9i3.30217.

32. Kromberg, J., Zwane, E., Manga, P., Venter, A., Rosen, E., Christianson, A. 2008. Intellectual disability in the context of a South African population. *Journal of Policy Practice in Intellectual Disabilities*. 5(2):89–95. doi:10.1111/j.1741-1130.2008.00153. x.

33. Lewis, D.D., Shaffer, J.R., Feingold, E., Cooper, M., Vanyukov, M.M., Maher, B.S. Slayton, R L. & et al. 2017. Genetic Association of MMP10, MMP14, and MMP16 with Dental Caries. *International Journal of Dentistry.* 2017, Article ID 8465125, 7 pages. doi.org/10.1155/2017/8465125

34. Malvania, E., Sheth, S., Sharma, A., Mansuri, S., Shaikh, F. & Sahani, S. 2016. Dental caries prevalence among type II diabetic and nondiabetic adults attending a hospital. *Journal of International Society of Preventive and Community Dentistry*. 6(Suppl 3):232-236. doi:10.4103/2231-0762.197202.

35. Mansell, J. 2006. Deinstitutionalisation and community living: progress, problems and priorities. *Journal of Intellectual & Developmental Disability*. 31(2):65–76. doi:10.1080/13668250600686726.

36. Maulik, P., Mascarenhas, M., Mathers, C., Dua, T., Saxena, S. 2011. Prevalence of intellectual disability: A meta-analysis of population-based studies. *Research in Developmental Disabilities*, 32(2):419-436.

37. May, P., De Vries, M., Marais, A.S., Kalberg, W., Buckley, D., Adnams, C., Hasken, J., Tabachnick, B., et al. 2017. Replication of high fetal alcohol spectrum disorders prevalence rates, child characteristics, and maternal risk factors in a second sample of rural communities in South Africa. *International Journal of Environmental Research and Public Health*. 14(5):522. doi:10.3390/ijerph14050522.

38. Minde, M. 1975. History of mental health services in South Africa. *South African Medical Journal*. 49(45):1890–1894.
39. Molteno, C., Smart, R., Viljoen, D., Sayed, R. & Roux, A. 1997. Twenty-year birth prevalence of Down syndrome in Cape Town, South Africa. *Paediatric and Perinatal Epidemiology*. 11(4):428–435.
40. Morgan, J.P., Minihan, P.M., Stark, P.C., Finkelman, M.D., Yantsides, K.E., Park, A., Nobles, C.J., Tao, W. & et al. 2012. The oral health status of 4,732 adults with intellectual and developmental disabilities. *Journal of the American Dental Association)*. 143(8):838–846.
41. Nemutandani, M.S., Adedoja, D. & Nevhuhlwi, D. 2013. Dental caries among disabled individuals attending special schools in Vhembe district, South Africa. *South African Dental Journal.*.68(10):458–461.
42. Nibali, L., Di Iorio, A., Tu, Y.K., Vieira, A.R., 2017. Host genetics role in the pathogenesis of periodontal disease and caries. *Journal of Clinical. Periodontology*. 44 Suppl 18, S52–S78. doi.org/10.1111/jcpe.12639
43. Nirje, B. 1994. The normalization principle and its human management implications. *International Social Role Valorization Journal*. 1(2):19–23.
44. Njenga, F. 2009. Perspectives of intellectual disability in Africa: epidemiology and policy services for children and adults. *Current Opinion in Psychiatry*. 22(5):475–461.
45. Nyland, E. 2002. *The Maleus Malificorum: Summation of the Maleus Malificorum*. Available: http://www.bibliotecapleyades.net/cienciareal/cienciareal12.htm [2016, January 19].
46. Opal, S., Garg, S., Jain, J. & Walia, I. 2015. Genetic factors affecting dental caries risk. *Australian Dental Journal*, 60(1):2-11.
47. Patel, V., Simbine, A.P.F., Soares, I.C., Weiss, H.A., Wheeler, E. 2007. Prevalence of severe mental and neurological disorders in Mozambique: a population-based survey. *Lancet*. 370(9592):1055–1060.
48. Petersen, I., Bhana, A., Campbell-Hall, V., Mjadu, S., Lund, C., Kleintjies, S., Hosegood, V., Flisher, A.J., et al. 2009. Planning for district mental health services in South Africa: a situational analysis of a rural district site. *Health Policy and Planning*. 24(2):140–150. doi:10.1093/heapol/czn049.
49. Petrovic, B.B., Peric, T.O., Markovic, D.L.J., Bajkin, B.B., Petrovic, D., Blagojevic, D.B., Vujkov, S. 2016. Unmet oral health needs among persons with intellectual disability. *Research in Developmental Disabilities*. 59:370–377. doi: 10.1016/j.ridd.2016.09.020
50. Petković, G. & Barišić, I. 2013. Prevalence of fetal alcohol syndrome and maternal characteristics in a sample of schoolchildren from a rural province of Croatia. *International Journal of Environmental Research and Public Health*. 10(4):1547–1561. doi:10.3390/ijerph10041547.
51. Rendall-Mkosi, K., London, L., Adnams, C., Morojele, N., McLoughlin, J. A., Goldstone, C. 2008. Fetal alcohol spectrum disorder in South Africa: situational and gap analysis. [Available at: https://www.unicef.org/southafrica/SAF_resources_fetalalcohol.pdf]
52. Reynalds, T., Zupanick, C. & Dombeck, K. 2015. *Early Medical Explanations of Intellectual Disability*. Available: https://www. mentalhelp.net/articles/early-medical-explanations-of-intellectual-disability/ [2016, January 20].

53. Roeleveld, N. and Zielhuis, G. 2008. The prevalence of mental retardation: a critical review of recent literature. *Developmental Medicine & Child Neurology*, 39(2):125-132.
54. Ropers, H.H.2010. Genetics of early onset cognitive impairment. *Annual Review of Genomics and Human Genetics*. 11:161-187. doi: 10.1146/annurev-genom-082509-141640
55. Rushton, P. 1988. Lunatics and idiots: mental disability, the community, and the poor law in North-East England,1660-1800. *Medical History*. 32(1):34–50.
56. Schneider, M., Claasens, M., Kimmie, Z., Morgan,R., Naicker, S., Roberts, A., McLarenet, P. 1999. *The extent of moderate and severe reported disability and nature of the disability experience in South Africa.* Commissioned by the Department of Health, Pretoria. Conducted by the Community Agency for Social Enquiry (CASE).
57. Seidman, L.J., Buka, S.L., Goldstein, J.M., Horton, N.J., Rieder, R.O., Tsuang, M.T. 2000. The relationship of prenatal and perinatal complications to cognitive functioning at age 7 in the New England cohorts of the national collaborative perinatal project. *Schizophrenia Bulletin*. 26(2):309–321.
58. Shereenberger, RC. A history of mental retardation. Baltimore: Brookes Publishing Co. 1983
59. Sherr, L., Mueller, J. & Varrall, R. 2009. A systematic review of cognitive development and child human immunodeficiency virus infection. *Psychology, Health & Medicine*. 14(4):387–404. doi:10.1080/13548500903012897.
60. Slayton, R. 2006. Genetics and environmental factors play important roles in the risk for periodontal disease and edentulism. *Journal of Evidence Based Dental Practice*, 6(3):238-239.
61. Stanley, B.O.C., Feingold, E., Cooper, M., Vanyukov, M.M., Maher, B.S., Slayton, R.L., Willing, M.C., Reis, S.E., & et al. 2014. Genetic Association of MPPED2 and ACTN2 with Dental Caries. *Journal of Dental. Research*. 93, 626–632. doi.org/10.1177/0022034514534688
62. Slayton,R.L., Cooper, M.E., & Marazita, M.L. 2005. Tuftelin, mutans streptococci, and dental caries susceptibility. *Journal of Dental Research*. 84(8): 711-714.
63. Statistics South Africa.2005. Census 2001-Prevalence of disability in South Africa. Available at: http://bethesdahoutbay.co.za/documents/CENSUS%202001%20REPORT.Disabilities%20in%20South%20Africa.pdf
64. Statistics South Africa. 2007. *Statistical Community Survey, 2007 (Revised Version)*. Available at: https://www.statssa.gov.za/publications/P0301/P0301.pdf
65. Statistics South Africa. 2014. *Census 2011: Profile of persons with disabilities in South Africa Available* at:. http://www.statssa.gov.za/publications/Report-03-01-59/Report-03-01-592011.pdf
66. Tassé, M.J., Luckasson, R. & Nygren, M. 2013. AAIDD proposed recommendations for *ICD–11* and the condition previously known as mental retardation. *Intellectual and Developmental Disabilities*. 51(2):127–131. doi:10.1352/1934-9556-51.2.127.
67. Trihandini, I., Wiradidjaja Adiwoso, A., Erri Astoeti, T., Marks, L. 2013. Oral health condition and treatment needs among young athletes with intellectual disabilities in Indonesia. *International Journal of Paediatric Dentistry.* 23(6):408–414. doi:10.1111/ipd.12010.

68. Urban, M.F., Stewart, C., Ruppelt, T., Geerts, L. 2011. Effectiveness of prenatal screening for Down syndrome on the basis of maternal age in Cape Town. *South African Medical Journal*. 101(1):45–48.
69. van Well, G.T.J., Paes, B.F., Terwee, C.B., Springer, P., Roord, J.J., Donald, P.R., van Furth, A.M., Schoeman, J.F. 2009. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the Western Cape of South Africa. *Pediatrics*. 123(1): e1–e8. doi:10.1542/peds.2008-1353.
70. Western Cape Government. 2006. *Valkenberg Hospital: The New Admission Unit*. Available: https://www.westerncape.gov.za/news/valkenberg-hospital-new-admission-unit [2016, January 01].
71. Whitaker, S. 2008. Intellectual disability: a concept in need of revision? *British Journal of Development Disabilities*. 54(106):3–9. doi:10.1179/096979508799103350.
72. Williams, A.N. 2002. "Of stupidity or folly": Thomas Willis's perspective on mental retardation. *Archives of Disease in Childhood*. 87(6):555–558.
73. Winter, K., Baccaglini, L. & Tomar, S. 2008. A review of malocclusion among individuals with mental and physical disabilities. *Special Care in Dentistry.* 28(1):19–26. doi:10.1111/j.1754-4505.2008.00005. x.

CHAPTER 3: PROJECT DESIGN AND METHODOLOGY

Introduction

This chapter provides an outline of the design and methodology of the investigation. It describes the target population, the methods and tools that were used to obtain data, explains the inclusion and exclusion criteria and defines the measurements which were used. The study aimed to determine the dental needs of children with ID at six special educational facilities (SE Facilities) in the Western Cape and Red Cross War Memorial Children's Hospital (RXH), South Africa. The first part of the investigation was conducted at the SE Facilities and the second part at the RXH. The influence of an external source of funding at the SE Facilities on the oral health needs of children was also explored.

3.1 Study design

The study was conducted using a cross-sectional, quantitative, exploratory descriptive design. Quantitative research is the investigation of a particular issue or issues by collecting numerical information followed by statistical analysis (Aliaga & Gunderson, 2000; Creswell, 2013). In the present study, a standardized sheet was used to gather information at the target sites in Cape Town. Following statistical evaluation, the results were compared to the outcomes of similar local and international investigations.

A second component of the investigation involved qualitative information. Qualitative research discusses various aspects of a specific investigation, including its significance, explanations and features (Berg, 2001). In the present investigation, material gathered during informal conversations between the author and the participating children's parents or caregivers was documented without further analysis. Using and integrating both quantitative and qualitative data in a single study is referred to as "mixed method" research (Wisdom &

Creswell, 2013). However, the present study did not conform to this definition and can be viewed as predominantly quantitative with a minor qualitative component.

The current investigation could also be regarded as "explorative descriptive" in nature because it recorded the unmet dental needs of children with ID at the various sites and described each comprehensively. Exploratory research investigates explicit aspects of an area of research, and its purpose is to recognize new aspects, comprehensions and to explore issues related to the subject rather than to deliver conclusive solutions to research problems (Dudovskiy, 2016). This investigatory technique also comprehensively examines relevant factors to formulate an apt portrayal of the prevalent conditions (Brink & Wood, 1998). The author considered this method to be suitable for acquiring an understanding of the unmet dental needs of children with ID in Cape Town, the challenges pertaining to dental management and the barriers that children with ID may meet when attempting to access oral health care.

Descriptive research describes meanings or features of occurrences and is used to identify difficulties with existing practice, justify the current practice, draw conclusions, or discover what is being or has been done (by others) in comparable circumstances (Waltz & Bausell, 1981). According to Uys & Basson (1991), an exploratory descriptive research design is flexible and provides an investigator with an opportunity to scrutinize all the characteristics of a problem being investigated.

3.2 Study sites

The 6 SE Facilities were: Belporto, Mary Harding, Blouvlei, Lentegeur, Agape and Beacon schools for children with intellectual disabilities. These schools are located in an area known as the "Cape Flats", a low-lying area on the periphery of the metropolis of Cape Town.

There were no ethnic barriers to admission and all schools enrolled children from diverse ethnic and cultural backgrounds. The schools were located in communities that were primarily of Cape Mixed Ancestry (admixture of indigenous San and Xhoi Xhoi with genetic contributions from Indonesia, Europe, the Indian subcontinent and sub-Saharan Africa). The socioeconomic profile of people living in the Cape Flats varies and 13.1% were unemployed in 2011 (Western Cape Provincial Treasury, 2012). The six schools were nominated for logistical reasons and because all new participants received thorough diagnostic assessment and psychological screening prior to admission. Access was dependent on the proximity of parents' residence to the school. All schools received financial assistance from the state (Department of Education, Western Cape Government) and one of the schools received additional funding from external private sources.

Nursing care was offered at each of the schools, but none had dedicated dental services. The parents occasionally arranged tooth extractions and other minor dental procedures in the private or state sectors, but many children lacked care of this type.

The second part of the investigation was undertaken at RXH (Fig 3.1). This is the oldest and largest hospital devoted entirely to child health in Southern Africa established in 1956.

Fig 3.1 Red Cross Children's Hospital

The hospital is subsidized by the State and receives external funding from various sources. The focus at the RXH is specialized health care for children and receives academic input from the University of Cape Town. Children with genetic causes of ID are referred to the Medical Genetic Clinic at the RXH from primary health care facilities for diagnostic assessment. In this clinic the parents are provided with information pertaining to the child's condition. A collaborative dental genetics facility conducted by the University of the Western Cape and the University of Cape Town was available for the investigation and management of children with oro-facial disorders (UWC-UCT dental genetics clinic; Fig 3.2).

Fig 3.2 The resident dentist at the RXH

3.3 Study Population

The study population consisted of children with ID attending 6 SE Facilities and children referred to the UWC-UCT Dental Genetics clinic.

3.3.1 Methods of referral

Special Educational Facilities

A clinical team from the Division of Human Genetics, University of Cape Town (UCT) regularly visited the schools for diagnostic assessment of the participants to determine possible genetic causes of children's disabilities. A resident staff member at each school selected the children with ID for medical and genetic evaluation. The team was accompanied by a qualified dentist (TR) in order to carry out dental assessments.

The participants from RXH were referred from the Medical Genetics unit, RXH to the UWC-UCT dental clinic for evaluation and treatment.

3.3.2 Methods of sampling

The technique used to recruit children for the investigation was termed “purposive sampling”, and in particular, a subgroup referred to as “homogenous sampling”. Purposive sampling is non-probability sampling in which the investigator selects participants or study units based on the characteristics of a population and the objective of the investigation (Dudovskiy, 2016). The subgroup of homogenous sampling refers to instances where all the participants of a specific sample have similar characteristics such as the same medical condition (Saunders, Lewis & Thornhill, 2015). This sampling method was used because of the accessibility to the target population of children and to comprehensively describe and understand their dental needs.

3.3.3 Inclusion criteria

Children with ID attending the SE Facility the day on which the team from the Division of Human Genetics, UCT visited the school to conduct diagnostic evaluation, were included in the first part of the study. The second part of the study included children with genetic ID syndromes referred from the Medical Genetics Unit, RXH to the UWC-UCT dental genetics clinic. To participate in either study, children, parents or caregivers were requested to give written consent or assent.

3.3.4 Exclusion criteria

In both studies, children whose parents had not given written consent and those who themselves had not assented to evaluation, were excluded.

3.4 Sample Size

All children evaluated by the genetics team at the target sites who were referred for dental evaluation were included in the sample. The sample size was determined by the number of children referred from the Division of Human Genetics and those seen at the special schools. One hundred and fifty-seven children from the SE Facilities and 49 children from the RXH constituted the final sample size.

3.5 Informed consent

The purpose, procedures and benefits of the study were explained to all participants, their parents or caregivers in their language of choice. The anticipated benefits of a dental examination and treatment were emphasized and the long-term advantages for children with ID were explained. The decision to participate was voluntary and the participants were allowed to withdraw from the study at any stage without the risk of forfeiting dental treatment. The author was proficient in two official languages (Afrikaans and English) and explained the procedures to the participants. A translator was available for children, parents and caregivers who required information in isiXhosa. Confidentiality was ensured at all times. The information was provided in writing to each participant and parent. (addendum 2).

Where possible, written informed consent was obtained from participants. When children were unable to give written consent as a result of their disability or age, consent was sought from their parents or caregivers and assent was obtained from children. The permission documents were standardized and printed in English, Afrikaans and isiXhosa. (English permission document - addendum 3). Any illustrative material such as photographs and radiographs included in this study was used with written consent.

3.6 Screening procedure

In both investigations the author undertook orodental screening of the children, and each child's medical and dental history was obtained and documented. Children at the SE Facilities were assessed using an office chair, natural light and a mouth mirror. Dental examinations at the RXH were performed in the dental chair using an overhead light and a mouth mirror. Strict infection control practices according to the guidelines proposed by the Centres of Disease control (CDC, 1986) were adhered to throughout the study by the use of gloves, masks and autoclaved instruments. In order to prevent the spread of infection and as a result of the high frequency of undiagnosed HIV infection in South Africa (chapter 14), all children examined were treated as if they were retroviral positive. These precautions were in keeping with the protocol followed by the Faculty of Dentistry, UWC.

When clinically indicated and when possible, panorex radiographs and lateral skull radiographs were obtained. When necessary clinical photographs were taken. The author arranged for any necessary dental treatment at one of the three dental clinics of the Faculty of Dentistry, UWC for both routine and specialized dental treatment.

3.7 Measurements

The oral screening was undertaken on all children who met with the inclusion criteria. The oral screening followed an adapted protocol formulated by the Special Olympics Special Smiles (SOSS) (White, Beltran & Perlman, 2004). Demographic (independent) variables included age, gender, disability, school and type of funding received by the school. Categorical dependent data included decayed, filled and missing teeth; gingival disease; malocclusion; craniofacial abnormalities and structural abnormalities of teeth.

Definition of variables

Untreated dental caries was diagnosed when at least one area of cavitation larger than 0.5mm was found in either the deciduous or the permanent dentition. “Missing teeth” were recorded if at least one tooth was absent at the time of examination. Variation in the outline and texture of the gingiva in at least three teeth was categorized as a “gingival disease”. “Dental fillings” referred to teeth that had been reconstructed in response to dental caries (White, Beltran & Perlman, 2004). The term “occlusion” describes the relationship of teeth of the maxilla to those of the mandible when they come into contact during function. “Malocclusion” refers to an inappropriate relationship between the teeth of the two dental arches when the jaws are closed. Obvious clinical changes in the facial bones including midface hypoplasia, mandibular prognathism and repaired clefts were included in the category “anomalies of the midface and jaw”. In the context of this thesis, the author included several types of morphological tooth anomalies under the broader heading of “structural abnormalities of teeth”. These included clinically evident variations in the size and appearance of teeth.

Based on the author’s empirical experience, qualitative information was collected on the children’s examination sheets regarding informal conversations about any difficulties parents or caregivers may have experienced in accessing oral health care for affected children.

3.8 Data Collection

The dental information was detailed on a specifically designed data collection sheet (addendum 2) and transferred to a spreadsheet in Microsoft Excel 2010. The information was categorized, coded and stored on the author’s personal computer where it was password protected thereby ensuring the confidentiality of participants’ information

3.9 Statistical Analysis

The collected data were transferred from the spreadsheet and analysed using STATA /IC 15.0 (StataCorp, USA). Categorical data was evaluated using a Chi-square test, and if assumptions were not satisfied, a Fisher's exact test was preferred. The Spearman's correlation coefficient was used to measure the strength of the relationship between individual parameters and and also between age groups and gender. In the sample this relationship is indicated by the symbol "r_s". The strength of the correlation using the following guide for the absolute value of: r_s: 00- 0.19 "very weak"; r_s: 0.20-0.39 "weak"; r_s :0.40-0.59 "moderate"; r_s :0.60-.79 "strong"; r_s :0.80-1.0 "very strong". A p-value < 0.05 rendered statistical significance.

3.10 Ethical and legal considerations

Both parts of the study were carried out in agreement with the Declaration of Helsinki, the Hippocratic Oath and the Singapore Statement on Research Integrity. The investigations commenced after ethical approval was obtained from the University of Cape Town's ethics committee (HREC reference number: 204/2013) (addendum 4).

3.11 Institutional collaboration

This study provided a platform for academic collaboration between the Faculty of Dentistry, University of the Western Cape (UWC) and the Division of Human Genetics, University of Cape Town (UCT). Subsequent to this study, there was an increase in the number of children who were referred from the Human Genetics clinic to the Dental Clinic at RXH. Regular consultation between the author and staff of UCT was a major factor in this project.

3.12 Social value

The participants of the investigation received dental consultations and treatments by qualified health professionals. Specialized dental services, otherwise not accessible to these children, were implemented. The dental services were also extended to the family members and caregivers of the children.

On request, the author continues to visit the SE Facilities to assess the oral health status of the participants and to arrange necessary treatment at the various facilities of the Faculty of Dentistry, UWC. Arrangements are also being made for oral disease prevention programmes at the schools where the children were educated.

References

1. Aliaga, M. & Gunderson, B. 2000. Interactive Statistics. *The Statistics Teacher Network*. 53:1–7. doi: 10.2307/40074316.
2. Berg, B.L. 2001. *Qualitative Research Methods for the Social Sciences*. 7th ed. Boston, United States of America: Pearson.
3. Brink, P.J. & Wood, M. 1998. *Advanced Design in Nursing Research*. 2nd ed, California, United States of America: SAGE Publications.
4. Centres for Disease Control. 1986. *CDC infection control for dentists*. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/00033634.htm [2015, April 14].
5. Creswell, J.W. 2013. *Research Design: Qualitative, Quantitative and Mixed Methods Approaches*. 4th ed. California, United States of America: SAGE Publications.
6. Dudovskiy, J. Ed. 2016. *An Ultimate Guide to Writing a Dissertation in Business Studies: A Step-by-Step Assistance*. Available: http://research-methodology.net/about-us/ebook/.
7. Saunders, M., Lewis, P. & Thornhill, A., 2015. *Research Methods for Business Students.* 6th Ed. London, United Kingdom: Pearson.
8. Uys, H.H.M. & Basson, A.A. 1991. *Research methodology in nursing*. 2nd ed. Pretoria, South Africa: Haum.
9. Waltz, C.F. & Bausell, R.B. 1981. Nur*sing Research: Design, Statistics, and Computer Analysis.* Philadelphia, United States of America: F.A. Davis Co.
10. Western Cape Provincial Treasury. 2012. Regional Development Profile: City of Cape Town Working paper.57.Available at: https://www.westerncape.gov.za/assets/departments/treasury/dc0_city_of_cape_town_sep-lg_profile_02_2013.pdf
11. White, J.A., Beltran, E.D. & Perlman S. 2004. Training Manual for Standardized Oral Health Screening Training Manual for Standardized Oral Health Screening. Availble: http://media.specialolympics.org/resources/health/disciplines/specialsmiles/Special-Smiles-Training-Manual.pdf.
12. Wisdom, J. & Creswell, J.W. 2013. Mix*ed Methods: Integrating Quantitative and Qualitative Data Collection and analysis while studying patient-centered medical home models. A*vailable: https://pcmh.ahrq.gov/sites/default/files/attachments/MixedMethods_032513comp.pdf

CHAPTER 4: PROJECT FINDINGS: Special Institutions

Introduction

The dental findings pertaining at the 6 SE Facilities are documented in this chapter. Each clinical parameter was compared to the age and gender of the affected child. A single school received an external source of funding and the dental findings at this school was compared to the schools that relied solely on State Funding. The association between variables among different age groups and genders were also recorded.

Oral investigation was undertaken in 167 children attending six SE Facilities in Cape Town. Reluctant participants were excluded from the investigation. The distribution of participants per school is recorded in Table IV.1. Overall, there were 107 (67%) males and 52 (33%) females and the average age was 10.1 years. Thirty-seven children (23.6%) were included in the 3-8-year-old age group; 57 (36.3%) in the 9-11-year-old age group and 63 (40.1%) in the 12-21-year-old age group.

Table IV.1: Distribution of participants per school

School	Number of participants (n)	Percentage of participants (%)
Mary Harding	60	38.3
Beacon	16	10.2
Belporto	38	24
Lentegeur	11	7
Blouvlei	14	9
Agape	18	11.5

The 106 participants (67.5%) with untreated dental caries [Table IV.2; Fig 4.1] were classified according to age categories 3-8 year-olds, n=25 (23.6%); 9-11 year-olds, n=42 (39.6%) and 12-21 year-olds, n=39 (36.8%) [Table IV.2; Fig 4.2]. Group sizes were unequal. There was no significant differences in the proportions in any of the age groups (*p*=0.167). There were 40 females (37.7%) and 66 males (62.3%) who were affected by untreated dental caries. There was, however, no significant differences in the proportions of untreated dental caries between genders (*p*=0.225).

Table IV.2: Number and Percentage of participants with Caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities and Jaw and Anomalies of the Midface per Age Group and Gender

	Untreated dental Caries		**Gingival Disease**		**Missing Teeth**		**Malocclusion**		**Structural Tooth Abnormalities**		**Anomalies of the Jaw and Midface**	
AGE GROUPS	**N**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**	**n**	**%**
3 - 8 year olds	25	23.6	24	22.1	20	27.4	7	15.6	1	9	11	16
9 - 11 year olds	42	39.6	43	45.2	33	45.2	14	31.1	4	36.6	32	46.4
12 – 21 year olds	39	36.8	41	31.9	20	27.4	23	53.3	6	54.4	26	37.6
	106		108		73		44		11		69	
GENDER												
Female	40	37.7	38	35.2	30	40.1	16	35.5	6	54.5	25	36.2
Male	66	62.3	70	64.8	43	59.9	2	64.6	5	45.5	44	63.8

Fig 4.1 Prevalence of participants with Untreated Dental Caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities, Anomalies of the Jaw and Midface and Fillings.

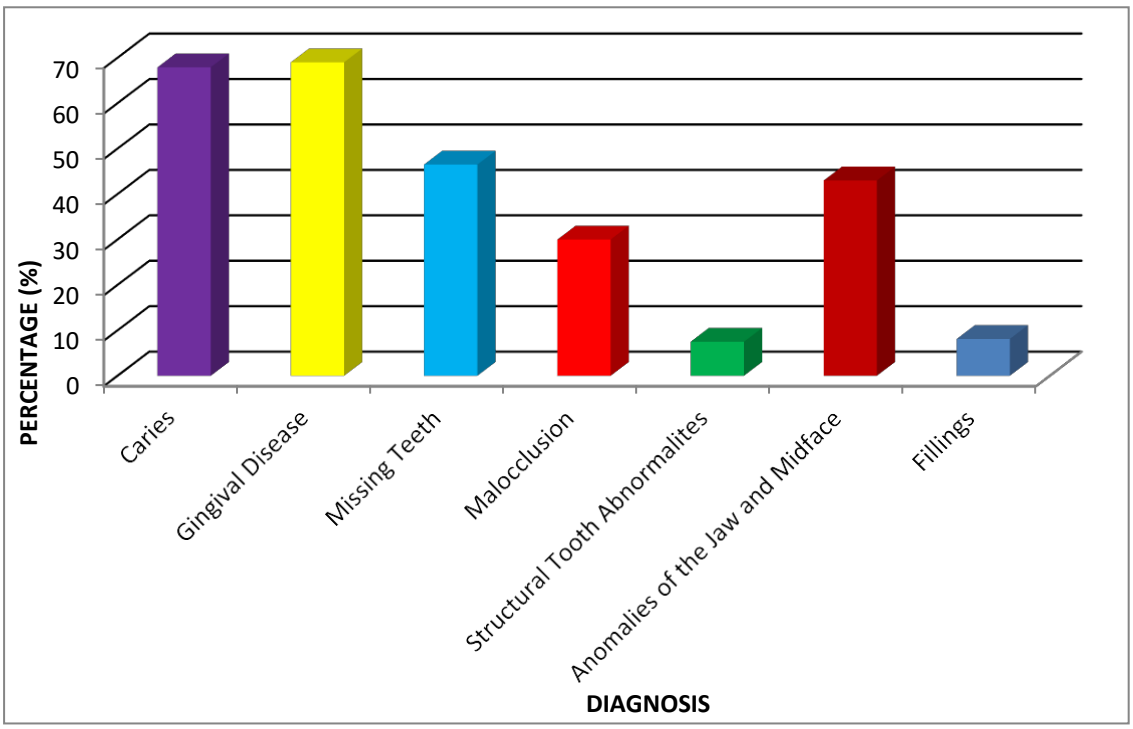
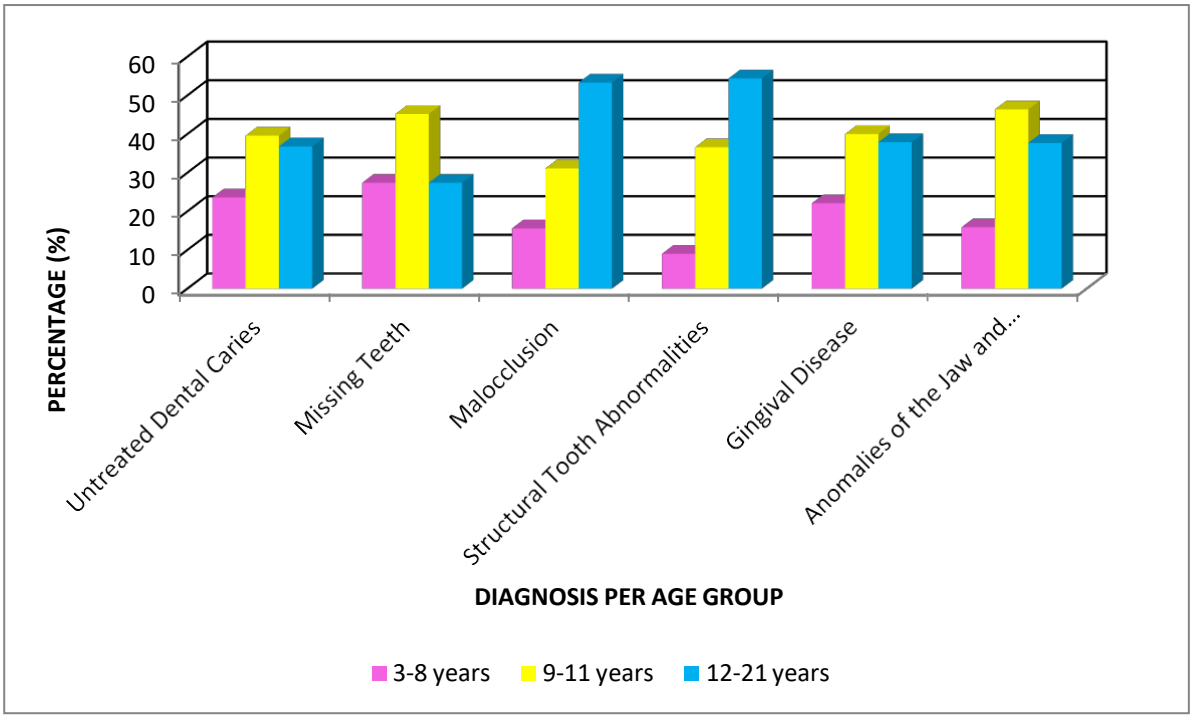


Fig 4.2 Prevalence of participants with Untreated Dental Caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities, Anomalies of the Jaw and Midface and Fillings per age group



Untreated dental caries showed a weak positive relationship with malocclusion (r_s=0.2, p=0.0002) and gingival disease (r_s=0.38, p=0.01) as well as a moderate positive correlation with missing teeth (r_s=423, p<0001).

Interestingly, the correlations between untreated dental caries and missing teeth among different age groups were also statistically significant. There was a moderate positive correlation between dental caries and missing teeth in 3-8 (r_s=0.512, p=0.001) and the 9-11 year-olds (r_s=0.459,p=0.0003) and a weak positive correlation between the two parameters in the 12-21 year-old age group (r_s =0.312, p=0.0133).

There was a very strong correlation between untreated dental caries and gingival disease (r_s=0.818, p<0.001) in the 3-8 year-old age group and a weak correlation between the variables in both the 9-11 year-old (r_s =0.307, p=0.0202) and 12-21-year-old (r_s =0.379, p=0.0023) age groups.

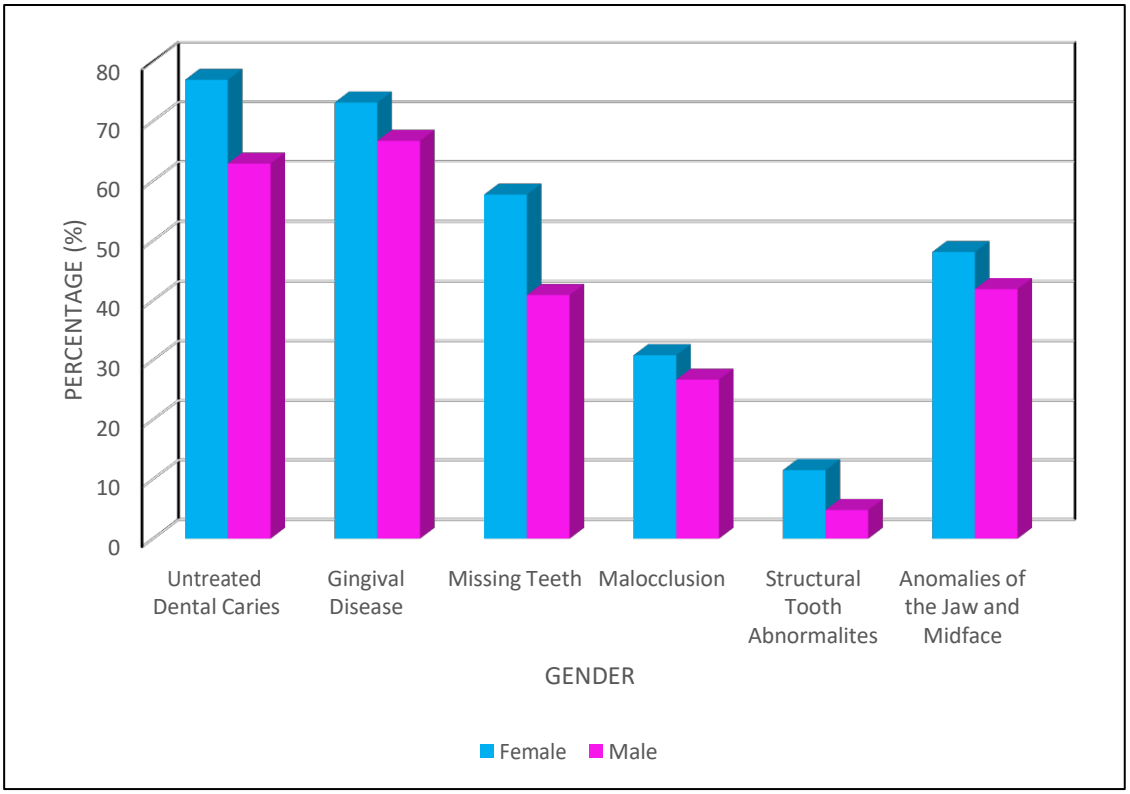
One hundred and eight participants (69%) with gingival disease [Fig 4.1 and Table IV.2] were categorized according to: 3-8 year-olds, n=24 (22.1 %); 9-11 year- olds, n=43 (40 %) and 12-21 year- olds, n=41 (37.9%)[Fig 4.1 and Table IV.2]. Group sizes were unequal. There was no significant differences in the proportion in any of these age groups as p = 0.259. Overall, there was a moderate positive correlation between gingival disease and missing teeth (r_s=423, p<0001) and a weak correlation between gingival disease and malocclusion (r_s=0.25, p=0.004). On further investigation, there was a strong correlation between gingival disease and missing teeth in the 3-8 year-olds (r_s=0.678, p<0.0001) and weak positive correlation between the two parameters in the 9-11 year-olds (r_s =0.339, p=0.009). There was also a

weak positive correlation between gingival disease and malocclusion in the 12-21 year-old age group (r_s=0.312, p=0.0134).

Seventy-three participants (46.5%) [Fig 4.1 and Table IV.2] without one or more teeth were classified into 3 age groups, 3 - 8 year-old, n = 20 (27.4 %); 9 - 11 year-old, n =33 (45.2%) and 12-19 year-old, n = 20 (27.4 %) [Fig 4.2 and Table IV.1]. There was a statistically significant difference in the proportion of participants with missing teeth across these age categories, $p < 0.007$. Post hoc analysis involved pairwise comparisons using the *z-test* of two proportions with a Bonferroni correction. The proportion of missing teeth in the 3 – 8 year-old category and the 12 -19 year-old age group were statistically significantly lower than the proportion of participants in the 9 -11 year-age group, $p = 0.008$.

Forty-five participants (28%) with malocclusion [Fig 4.1 and Table IV.2] were classified according to age categories: 3-8 year-olds, n = 7 (15.6 %), 9 -11 year-olds, n = 14 (31.1 %) and 12-21 year-olds, n = 24 (53.3%) [Fig 4.2 and Table IV.1]. Group sizes were unequal. There were no significant differences in the proportions of participants with malocclusion in any of these age groups as, $p = 0.083$. The prevalence of malocclusion was similar among females and males (p=0.797) [Fig 4.3]. There was a weak positive relationship between malocclusion and age (r_s=0.21, p=0.009) and anomalies of the jaw and midface (r_s=0.2963, p=0.0002). All these correlations were statistically significant.

Fig 4.3 Percentage of Untreated dental Caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities and Anomalies of the Jaw and Midface per Gender



Eleven participants (7%) with structural tooth abnormalities [Fig 4.1 and Table IV.2] were classified according to age categories: 3 – 8-year-olds, n = 1 (9 %), 9 – 11-year-olds, n = 4 (36.6 %) and 12 – 21- year old's, n = 6 (54.4%). Group sizes were unequal. There were no significant differences in the proportions of participants with structural tooth abnormalities in any of these age groups as, $p = 0.439$.

Sixty-nine participants (44 %) [Fig 4.1 and Table IV.2] with anomalies of the jaw and midface were classified into 3 age groups, 3 to 8 year-olds, n = 11 (16 %); 9 to 11 year-olds, n =32 (46.4 %) and 12 to 21 year- olds, n = 26 (37.6 %) [Fig 4.2 and Table IV.2]. There was a statistically significant difference in proportion participants with anomalies of the jaw and

midface across these age categories, p = 0.024. Post hoc analysis involved pairwise comparisons using the *z-test* of two proportions with a Bonferroni correction. The proportion of participants with anomalies of the jaw and midface in the 3 - 8 year-age group was statistically significantly lower than the proportion of participants in the 9 -11 year-age group, p =0.006. There was no statistically significant correlation between male (41.9%, n = 44) and female participants (48.1%, n = 25) who presented with anomalies of the jaw and midface [Fig 4. 3 and Table IV.2], p = 0.497

The correlations between various clinical parameters are listed in Table IV.3.

Table IV.3: Correlation of Untreated dental caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities and Anomalies of the Jaw and Midface

	Age	Untreated dental caries	Gingival Disease	Malocclusion	Anomalies of the Jaw and Midface
Untreated dental caries			r_s=0.38 ** p=0.01	r_s=0.2 ** p=0.0002	
Missing Teeth		r_s=0.423*** p<0001	r_s=0.43 *** p<0.001		r_s=0.17 * p=0.03
Malocclusion	r_s=0.19 * p=0.012		r_s=0.423 p<0.0001		r_s=0.29 ** p=0.002

* rs: 00-0.19 “very weak”

**rs: 0.20-.39 “weak”

*** rs: 0.40-0.59 “moderate”

Thirteen children (8.1%) of children had dental fillings.

There was no significant difference in the prevalence of the clinical parameters between the school that received additional private funding and those relying solely on the State’s non-

funded institutions, except for the prevalence of anomalies of the jaw and midface (36.1%, n = 43 vs 68.4%, and n = 26), $p = 0.0011$ [Table IV.4].

Table IV.4: Percentage of Caries, Gingival Disease, Missing Teeth, Malocclusion, Structural Tooth Abnormalities and Anomalies of the Jaw and Midface per Site and Funding

	Untreated Dental Caries		**Gingival Disease**		**Missing Teeth**		**Malocclusion**		**Structural Tooth Abnormalities**		**Anomalies of the jaw and Midface**	
	N	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
SITE												
Mary Harding (n=60)	43	74	45	75.0	25	41.7	19	31.7	3	5.0	20	33.3
Beacon (n=16)	9	69	10	62.5	9	56.3	2	12.5	1	6.3	5	31.3
Belporto (n=38)	26	72	28	73.7	22	57.9	13	34.2	5	13.2	26	68.4
Lentegeur (n=11)	10	91	6	54.6	3	27.3	1	9.1	0	0.0	4	36.4
Agape (n=18)	7	52	6	42.9	4	28.6	2	14.3	0	0.0	0	0.0
Blouvlei (n=16)	11	61	13	72.2	10	55.6	7	38.9	2	11.1	14	77.8
SCHOOL FUNDING												
Funded (n=38)	26	68.4	28	73.7	22	58.0	13	34.2	5	13.2	26	68.4
Non-Funded (n=119)	80	67.2	80	67.2	51	42.9	31	26.1	6	5.0	43	36.1

Summary of results:

The most common unmet dental needs among the participants at the SE Facilities were untreated dental caries and gingival disease. A weaker correlation existed between dental caries and missing teeth in the older participants (12-21 year old age group) than in the younger participants. Conversely, a stronger correlation between dental caries and gingival disease was found in the younger participants (3-8 year old age group).

Overall, there was a significant relationship between gingival disease and missing teeth and malocclusion. A correlation between gingival disease and missing teeth was documented in the two younger age groups of participants and a relationship between gingival disease and malocclusion was found in the older age category.

An association was determined between malocclusion and age and anomalies of the jaw and midface

Participants in the 9-11 age category lacked more teeth and was affected by more changes of the jaw and midface than both older and younger participants.

CHAPTER 5: PROJECT FINDINGS: Red Cross Children's Hospital

A total of 78 participants with genetic syndromes were referred from the Medical Genetics Unit at RXH for oral investigation and assessment. Thirty-six (46%) were boys and 42(54%) were girls. The average age was 9.5 (SD = 5.1) years. Their ages were: 3 to 8 years (n = 34 and 44%), 9 to 11 years (n = 17 and 22%), 12 to 21 years (n = 27 and 35%). The distribution of age group was similar for girls and boys, p = 0.20. Forty-nine (63%) of the participants were diagnosed with an ID syndrome. The remaining 29 were excluded from the investigation. Children with ID tended to be slightly older, mean (SD) = 10.6 (5.3) years compared to children without ID, 7.6 (4.0), p = 0.01. Only the participants with ID were included in the study.

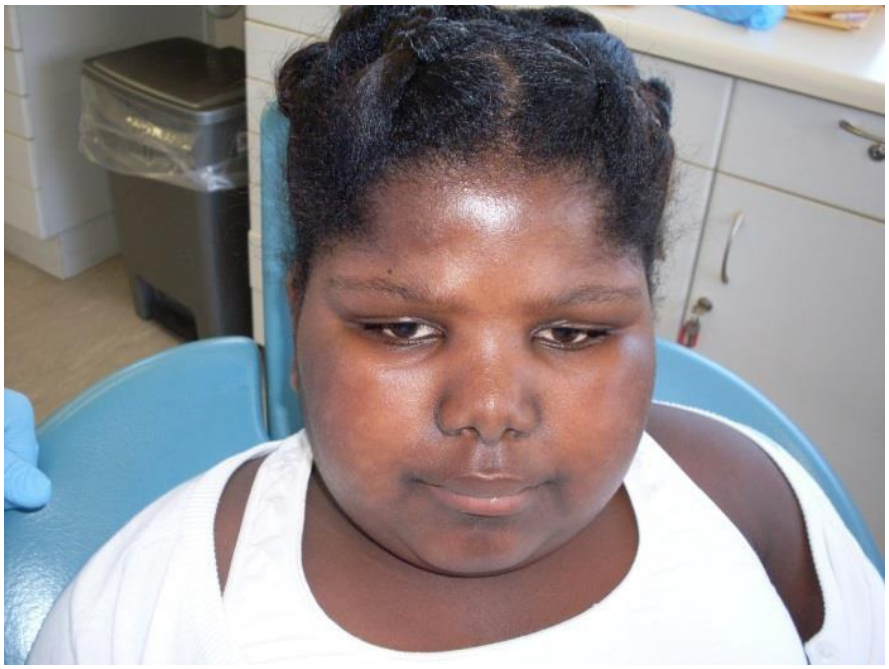


Fig 5.1 A girl aged 10 years with Bardet–Biedl syndrome

Fig 5.2 A boy aged 6 years with Rubinstein-Taybi syndrome with his unaffected sister

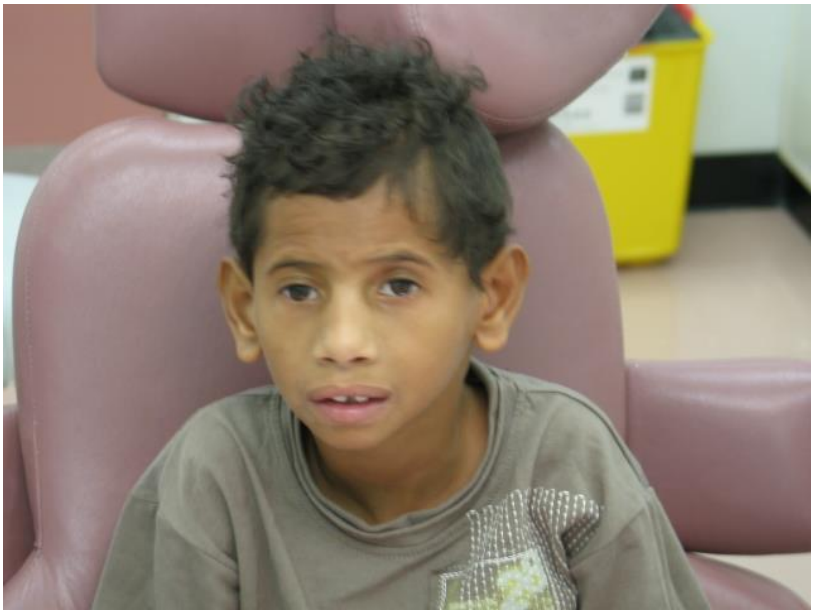


Fig 5.3 A boy with Seckel syndrome

Fig 5.4 (a) A girl aged 10 years with Turner syndrome

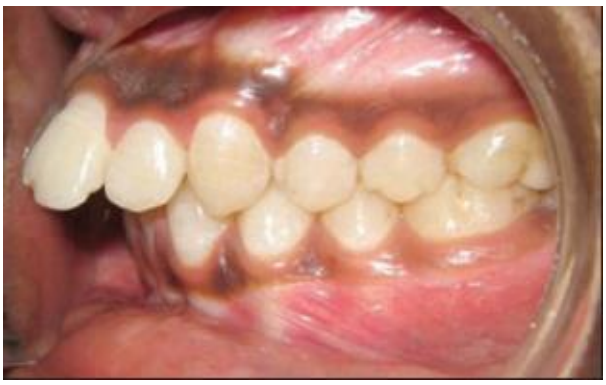


Fig 5.4 (b) Severe overjet was evident in this girl

Fig 5.5 A girl aged 4 years with Incontinentia Pigmenti.
Her dental anomalies are depicted in Fig 7.1

Fig 5.6 (a) A girl aged 11 years with the CANDLE syndrome She had an enlarged abdomen and wasting of her extremities.

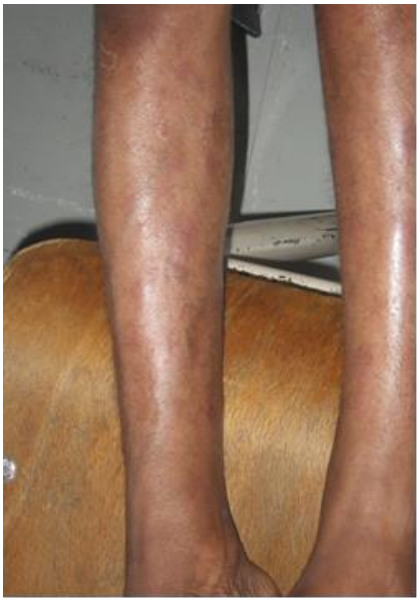


Fig 5.6 (b) Annular purpuric cutaneous plaques on her legs. Similar lesions were evident on her torso.

Fig 5.7 (a) A girl aged 17 years with Williams syndrome.

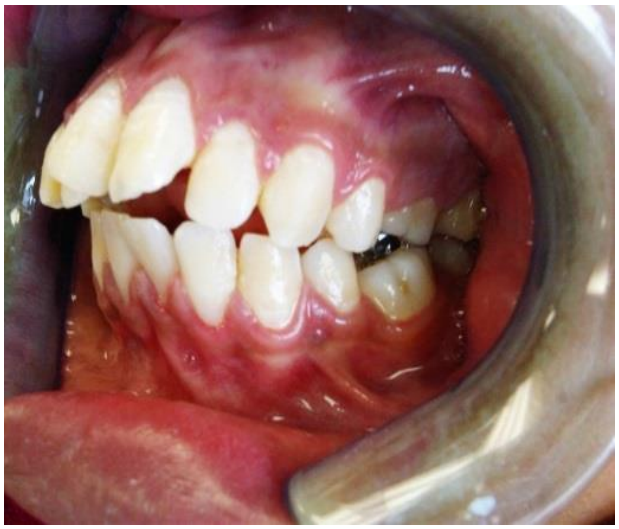


Fig 5.7 (b) Severe malocclusion was evident in the same girl

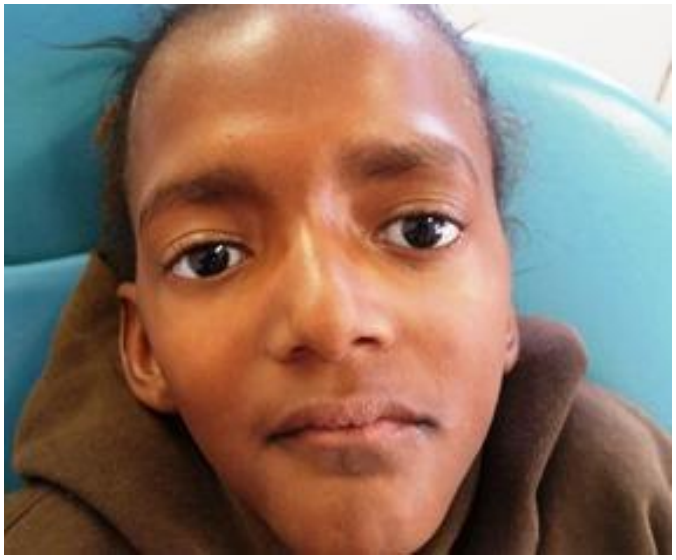


Fig 5.8 (a) A girl aged 11 years with an undiagnosed genetic ID syndrome with marfanoid features

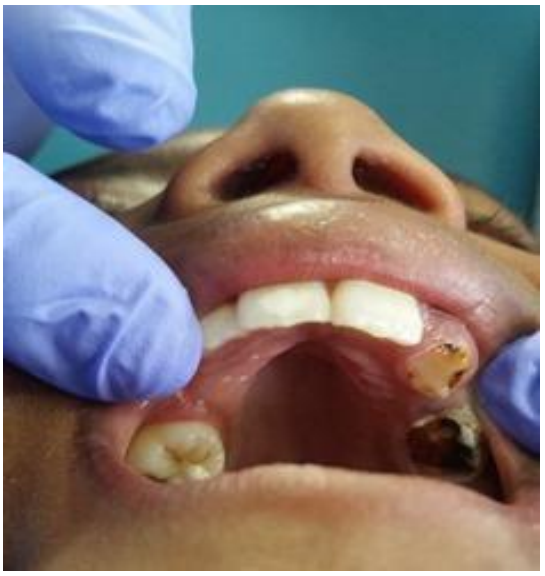


Fig 5.8 (b) She had a high arched palate and several carious teeth

Fig 5.9 (a) A boy aged 4 years with Trichorhinophalangeal syndrome. Sparse hair is noticeable on the scalp and eyebrows

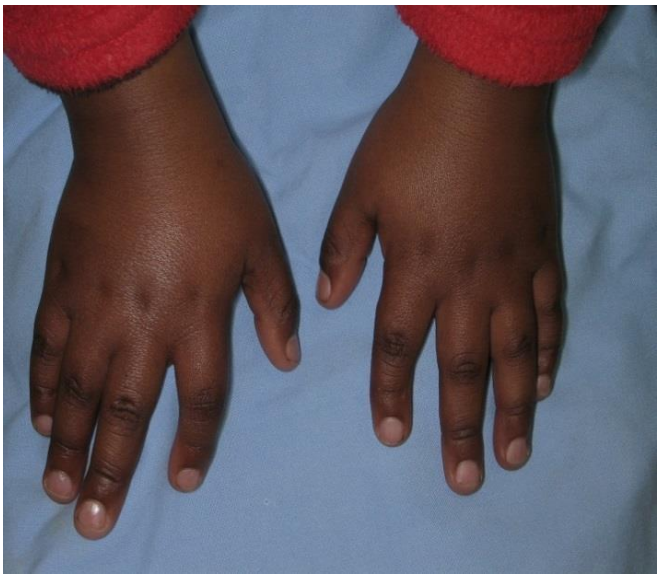


Fig 5.9 (b) Medial deviation of index fingers.

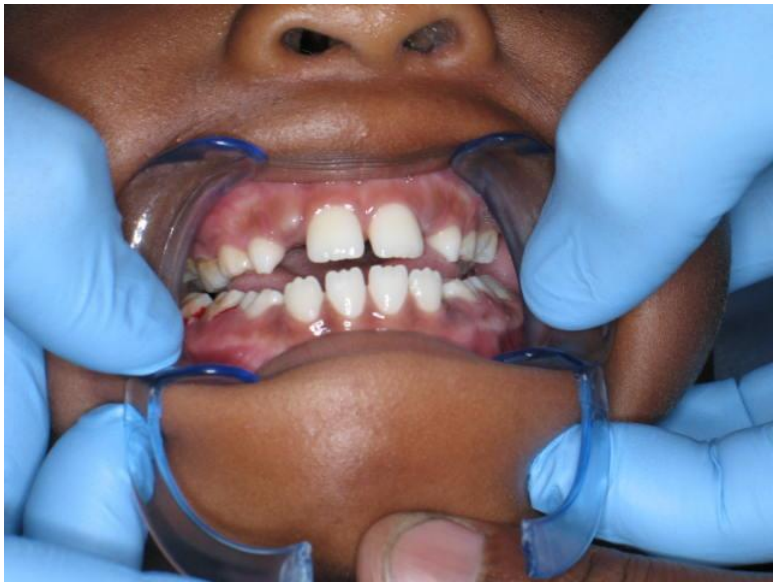


Fig 5.9 (c) Complete eruption of permanent central maxillary and mandibular incisors

Fig 5.10 (a). A girl with Prader-Willi syndrome

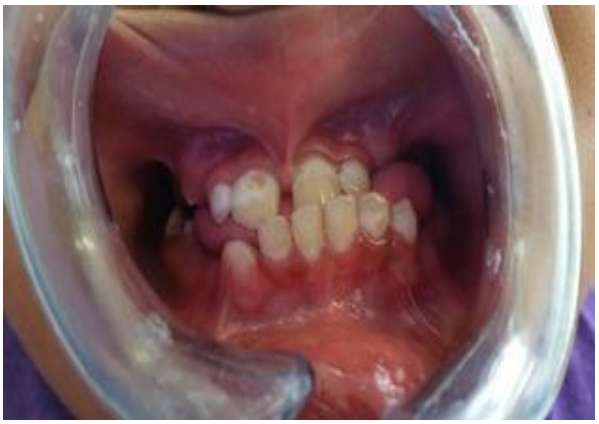


Fig 5.10 (b) She had significant enamel hypoplasia

Among the participants with ID, a total of 41 (84 %) had untreated dental caries [Table V.1; Fig 5.11]. These children were classified according to age categories 3-8 years, n=17 (41.5%); 9-11 years, n=7 (17 %) and 12-21year olds, n=17 (41.5 %) [Fig 5.12; Table V.1]. Group sizes were unequal. There were no significant differences in the proportions of affected and unaffected children in any of the age groups (p=0.893).

Fig 5.11: Prevalence of participants with Untreated Dental Caries, Gingival Disease, Missing Teeth, Malocclusion and Structural Abnormalities at RXH

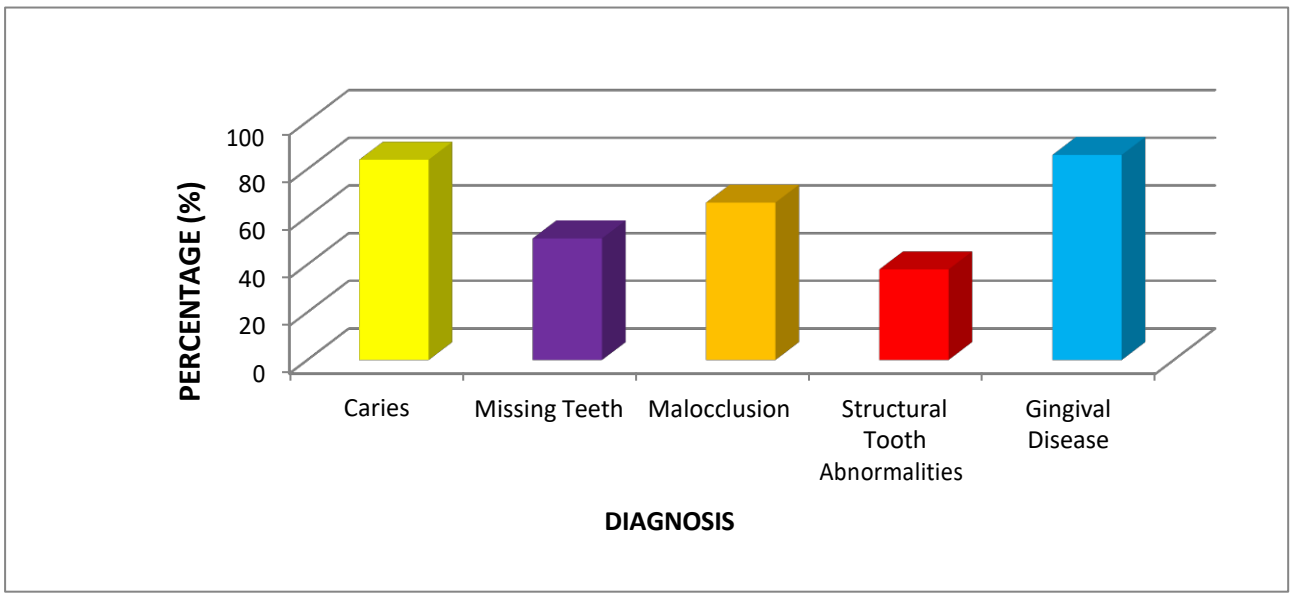
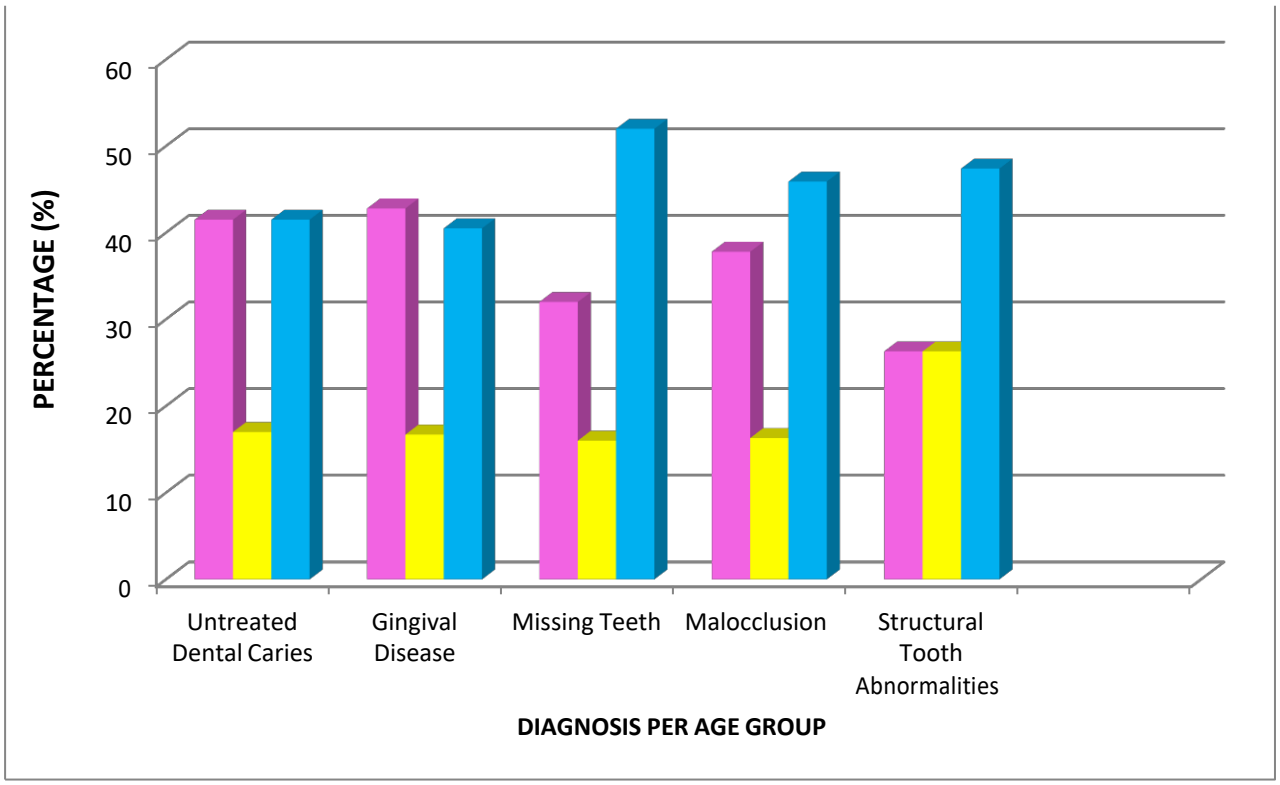


Table V.1: Percentage of participants with Untreated Dental Caries, Gingival Disease, Missing Teeth, Malocclusion and Structural Tooth abnormalities

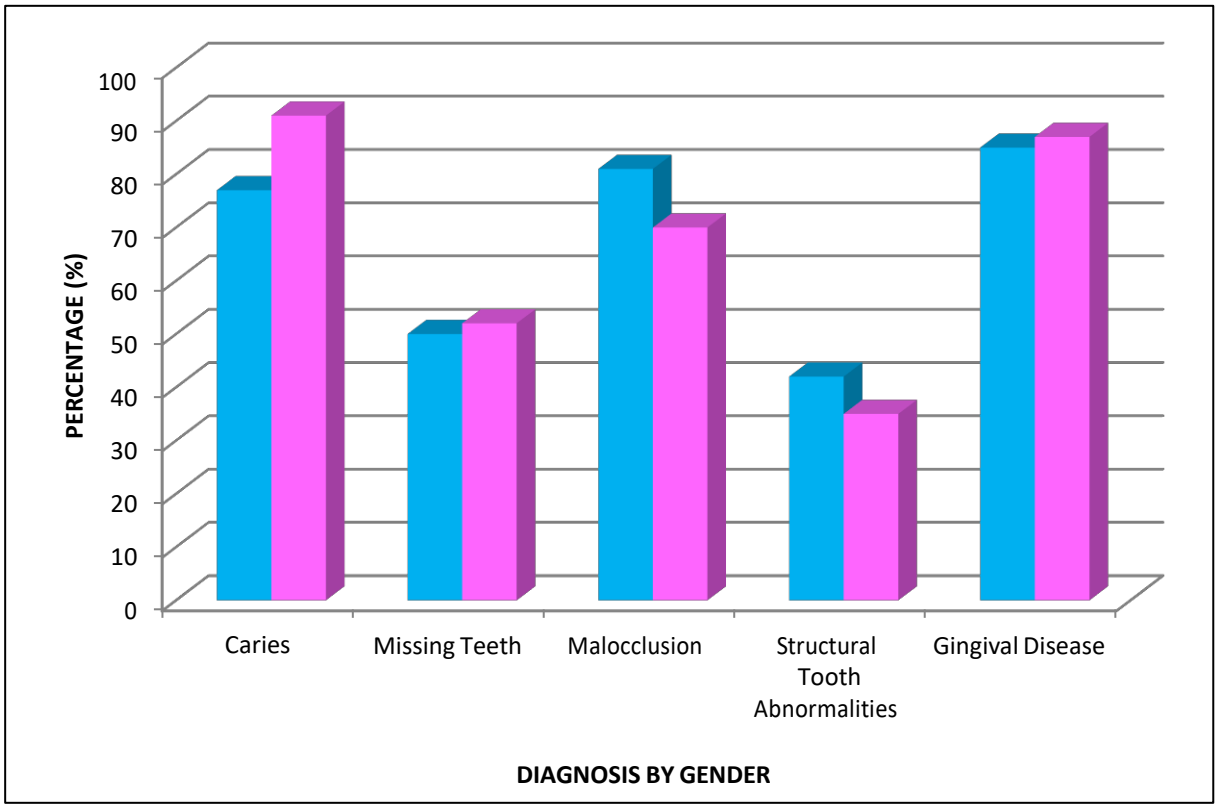
	Untreated Dental Caries		Gingival Disease		Missing Teeth		Malocclusion		Structural Tooth Abnormalities	
AGE	**N**	**%**	**N**	**%**	**N**	**%**	**n**	**%**	**n**	**%**
3 - 8 year olds	17	41.5	18	42.9	8	32	14	37.8	5	26.3
9 -11 year- olds	7	17	7	16.7	4	16	6	16.2	5	26.3
12 - 21 year olds	17	41.5	17	40.4	13	52	17	46	9	47.4
	41		42		25		37		19	
GENDER										
Female	20	48.8	22	52.4	13	52	21	56.8	11	57.9
Male	21	51.2	20	47.6	12	48	16	43.2	8	42.1
	41		42		25		37		19	

Fig 5.12 Percentage of participants with Untreated dental Caries, Gingival Disease, Missing Teeth, Malocclusion and Structural Tooth Abnormalities per Age Group



Twenty females (48.5%) and 21 males (51.2 %) [Table V.1; Fig 5.13] were affected by untreated dental caries. There was, however, no significant differences in the proportions of untreated dental caries between genders, as p=0.254 A weak positive correlation between untreated dental caries and gingival disease (r_s=0.370, p=0.012) was detected.

Fig 5.13 Percentage of Caries, Gingival Disease, Missing Teeth, Malocclusion and Structural Tooth Abnormalities by Gender



Forty-two (68%) of the study sample with gingival disease [Fig 5.11, Table V.1] were categorized according to: 3-8 year-olds, n=18 (42.9 %); 9-11 year- olds, n=7 (16.7 %) and 12-21 year- olds, n=17 (40.5 %) [Fig 5.12 and Table IV.1]. Group sizes were unequal. Although there were no significant differences in the proportion of gingival disease in any of these age groups (p = 0.259), participants in the 9-11 year age group had less gingival disease (n=7 and 16.7 %) compared with both the 3 – 8 (n=18 and 42.9%) and the 12-21 year-olds (40.4 % and

n=17) groups. This however, was not statistically significant (*p*=0.701). The proportion of the children with gingival disease was not influenced by gender (*p*= 0.815).

Twenty-five participants (51 %) [Fig 5.11, Table V.1] with ID and lacking one or more teeth. without one or more teeth were classified into 3 age groups, 3 – 8 year old, n = 20 (27.4 %); 9 – 11 year -old, n =33 (45.2%) and 12 – 19 year-old, n = 20 (27.4 %) [Fig 4.2 and Table IV.1]. There was a statistically significant difference in the proportion of participants without teeth across these age categories, $p < 0.007$. Post hoc analysis involved pairwise comparisons using *the z-test* of two proportions with a Bonferroni correction. The proportion of missing teeth in the 3 to 8-year-old category and the 12 -21year-old age group were statistically significantly lower than the proportion of participants in the 9 to 11-year age group, *p* =0.008.

Seventy six percent (n = 37) of participants with ID had with malocclusion [Fig V.11]. This was present in 37.8 % (n = 14) of children aged 3 – 8 years; in 16.2% (n=6) of the 9-11 year-old group and in 46% (n=17) of 12-21 year-olds [Fig V.12, Table V.1]. However, these differences were not statistically significant *(p*=0.717). There was no significant statistical relationship between the prevalence of malocclusion in males, 43.2% (n = 16) and females, 56.8% (n = 21), *p* = 0.508 [Fig 5.13, Table V.1].

Thirty-eight percent (n=19) of the study sample had structural abnormalities of their teeth

[Fig 5.11]. There was no statistically significant relationship between this parameter, gender and age group (*p*=0. 590 and *p*=0. 162) [Table V.1].

There was a definite but weak correlation between gingival disease and untreated dental caries, r_S=0.375, p=0.0102.

Only 11 children had fillings at the time of the investigation.

Comparison of the variables between RXH and the SE Facilities

One hundred and forty-six participants diagnosed with caries were classified according to the seven investigation sites. Group sizes were unequal. There were no significant differences in the proportions of dental caries among these sights p=0.06.

One hundred and forty-nine participants were classified as having signs of gingival disease across the 7 sites under investigation. At the conclusion of the investigation there was a statistically significant difference in the proportion of participants with malocclusion across the 7 sites, p = 0.036. Post hoc analysis involved pairwise comparisons using the *z-test* of two proportions with a Bonferroni correction. The proportion of participants with gingival disease at RXH was statistically significantly different compared to Lentegeur and Blouvlei schools, $p < 0.05$.

One hundred and forty-six participants with missing teeth were classified according to the seven sites under investigation. Group sizes were unequal. There were no significant differences in the proportions in any of these age groups as, p = 0.266.

Thirty participants at the seven investigation locations had structural tooth abnormalities. At the conclusion of the project, there was a statistically significant difference in the proportion of participants with structural tooth abnormalities, p = 0.001. Post hoc analysis involved

pairwise comparisons using the z-test of two proportions with a Bonferroni correction. The proportion of participants with structural tooth abnormalities at RXH was statistically significantly different compared to the SE Facilities sites, $p < 0.05$.

Eighty-two participants were classified as having malocclusion across the 7 sites under investigation. At the conclusion, there was a statistically significant difference in the proportion of participants with malocclusion at these locations, $p = 0.0001$. Post hoc analysis involved pairwise comparisons using the z-test of two proportions with a Bonferroni correction. The proportion of participants with malocclusion at RXH was statistically significantly higher compared to the SE Facilities, $p < 0.0001$.

Summary of results:

Dental caries and gingival disease were the most frequent untreated dental condition among participants at the RXH. There was a significant relationship between untreated dental caries and gingival disease.

Although the participants in the 9-11 age category had less gingival disease, this age group also lacked the most teeth. Apart from the relationship between untreated dental caries and gingival diseases, no further relationship between the remaining parameters were noted.

Conclusion:

Chapters 4 and 5 highlight the benefits of dentist-clinical geneticist collaboration for an optimal diagnosis and management; the clinical geneticist to assist in identifying isolated or syndromic features and the dentist to be cognizant of the signifance of inherited ID disorders. Furthermore, the collaborative association may benefit the dentist by familiarizing him\herself with concepts of inheritance patterns and basic genetic counselling principles.

SECTION 2

Artwork by : Mahesh Micahel Rugubar

CHAPTER 6: ACQUIRED ABNORMALITIES OF TEETH AND SUPPORTING STRUCTURES

Introduction:

This chapter focuses on the importance, risk factors and management of untreated dental caries and gingival disease in ID. The author integrates the results of the investigation at both the SE Facilities and the RXH into a comprehensive discussion to highlight the importance of the disorders and to arrive at a possible explanation of the results.

6.1 Untreated Dental Caries

The results of this study show that a significant proportion of the participants at the SE Facilities (67%) and the RXH (84%) had one or more untreated carious lesions of the teeth (Fig 6.1). There was no significant difference between the proportions of participants with untreated dental caries at the RXH and those attending the SE Facilities. These findings corroborate the results of previous investigations among children with ID in lower-middle-income countries (Shivakumar et al., 2018) and 6 and 12 year-old children in the general population of the Western Cape (Smit, Barrie&Louw., 2017). However, van Wyk & van Wyk, 2004; Cleaton-Jones & Fatti, 2009; Nqcobo, Yengopal, & Rudolf, 2012 reported a lower prevalence of untreated dental caries in similarly aged children in the broader South African community. Conflicting results were documented in investigations from other upper middle income and high-income countries (Dellavia et al., 2009; Anders & Davis, 2010; Fernandez et al., 2012; Leroy, Declerck & Marks, 2012). The outcome of this study highlights the extent of untreated dental caries among children with ID in Cape Town.

There are several possible reasons for the high prevalence of untreated dental caries in this investigation. One reasonable explanation could be that the participants may have lacked the

physical ability to accomplish or the mental capacity to comprehend the need for proper oral hygiene practices (Anders & Davis, 2010). Furthermore, co-existing conditions, including sensory disorders, anxiety and behavioural problems, may have prevented the participants from practising effective oral hygiene procedures (Cumella et al., 2000). Physical challenges that accompany ID such as the inability to rinse, oral aversion, and a tendency to gag may have precluded proper oral health care (Wiener, 2015).

Another explanation for the high prevalence of untreated dental caries in this study could be that the participants required the assistance of parents or caregivers to support their day-to-day oral health care practices. With several children displaying uncooperative and challenging behaviour, their dental needs may not have been a priority for the caregivers. Furthermore, brushing and flossing teeth of children with ID requires skill, and the parents or caregivers may have had lacked confidence in their ability to provide dental care for them (Minihan et al., 2014).

From another perspective, the high prevalence of dental caries among the children involved in the study, may have been due to the lack of access to essential oral health care services and the inadequate number of dental clinics and oral health professionals in the Western Cape. (Smit, Barrie & Louw,2017).

The children assessed at the RXH were all syndromic and attended multiple clinics for their systemic disorders. The high prevalence of untreated dental caries at this facility suggests that their general health concerns and syndromic complications may have overshadowed their oral health care. RXH is one of two tertiary paediatric institutions offering specialized care to children without medical insurance in South Africa. For this reason, children from different parts of the country, including rural towns, are referred to RXH for management of

their health care needs. Access to specialized and primary health care services, including dentistry, in these rural areas, are lacking and may have contributed to the high prevalence of dental caries among the participants at this site.

Apart from their cognitive and physical challenges, several additional factors may have contributed to the high prevalence of untreated dental caries experienced by the participants in the present series. Moreover**,** the motivation of caregivers to provide, supervise or implement the participants' routine dental care as well as their access to oral health care may have influenced the outcome of the investigation.

6.1.1 Risk factors for dental caries in children with ID

Children with ID are more susceptible to develop dental caries than non-ID children. Coexisting oral conditions such as hypoplastic enamel and poor nutrition play significant roles in enamel demineralization and caries formation (Liu et al., 2010; Alaki & Bakry, 2012). Difficulty in swallowing and the oral retention of food and fluids further increases the risk of developing dental decay. Furthermore, hyperactive gag reflexes and gastric reflux, often accompanying ID, can subject teeth to the acid environment of the stomach causing erosion of tooth enamel (Norwood & Slayton, 2013).

Preterm birth and extended periods of intubation during neonatal life in children with an ID may result in avoidance of textures and flavours of specific foods (oral aversions). Preferences for soft, sweet, sticky food not only cause nutritional deficiencies but can also have deleterious effects on the teeth. Processed and pulverized food containing refined sugar tends to remain on tooth surfaces longer than those with high fibre content. The continued

exposure of tooth surfaces to these fermentable carbohydrates results in a sustained acidic oral environment that favours enamel demineralization and dental caries.

6.1.2 Dental implications of untreated dental caries in ID

The local and systemic consequences of untreated dental caries reflect its importance in the well being of children with ID. Pain and discomfort are the most common immediate complications of dental caries. If not eliminated, the offending cariogenic bacteria can spread from the surface towards the pulp of the tooth. A further extension to the periapical region of the jaws could result in abscesses or cysts. In severe cases, when the body fails to localize bacterial invasion, sepsis may occur and involve the surrounding bone or soft tissue. These processes can have grave consequences such as cellulitis and osteomyelitis, which warrant emergency intervention. Extensive carious lesions may hinder speech, and inadequate mastication can result in malnutrition and bowel irregularities (Abanto et al., 2012). Untreated dental caries may also affect other oral structures. In the context of this investigation untreated dental decay was related to malocclusion (r_s=0.2, p=0.0002), gingival disease (r_s=0.38, p=0.01) and the absence of teeth (r_s=0.423, p<0001) at the SE Facilities and to gingival disease at the RXH (r_s=0.370, p=0.012).

The association between dental caries and malocclusion in the general population have been well-established (Duarte-Rodrigues et al., 2017; Disha et al., 2017; Sá-Pinto et al., 2018). Malocclusion and dental caries appear to have a reciprocative relationship. Malaligned or crowded teeth are difficult to clean and serve as a reservoir for cariogenic plaque and bacteria (Kirchberg, Treide & Hemprich, 2004). The inadequate mechanical removal of plaque and bacteria from these teeth increases the risk of dental caries. Conversely, dental caries can result in premature tooth loss that can predispose an individual to malocclusion.

Although there are several options available to restore decayed teeth, dental extractions are often the most accessible and affordable means to alleviate pain. As a result, this procedure is the most common cause of tooth loss in both the primary and permanent dentitions. This study demonstrated a moderate positive correlation between untreated dental caries and missing teeth (r_s=0. 423, p<0001) at the SE Facilities. The results imply that the linear relationship between untreated dental caries and missing teeth is relatively strong and therefore dental caries, apart from other factors, could be instrumental for the high frequency of missing teeth at these sites.

The association between untreated dental caries and the absence of teeth was stronger in the younger participants than those aged between 12 and 21 years. This trend suggests that tooth loss in the younger groups of children was more likely a consequence of dental caries and that other influences may have contributed to this phenomenon in their older counterparts.

Caries and periodontal disease, a complication of gingival disease are both microbial-based infections requiring the presence of plaque. In many instances, these infections often coincide (Merchant, 2012). This relationship was confirmed in the current study when a positive correlation between the two variables was established at both the SE Facilities (r_s=0.38, p=0.01) and the RXH (r_s=0.375, p=0.0102). Vehkalahti & Paunio, 1994 documented similar findings in 227 school children, as did Albandar et al., 1995 in 4,777 Finnish adults. The weakness of correlation established in this study could be explained by the fact that the gingival changes were confined to the superficial areas of the gum and did not extend to the periodontal apparatus in any of the participants.

The oral cavity is a source of numerous pathogens and children with comorbid disorders, such as cardiac defects, will benefit from good oral hygiene by the elimination of unnecessary sources of bacteria. In some instances, children with extensive carious lesions require a complete dental clearance before cardiac surgery to remove any dental infection, which could contribute to the development of bacterial endocarditis.

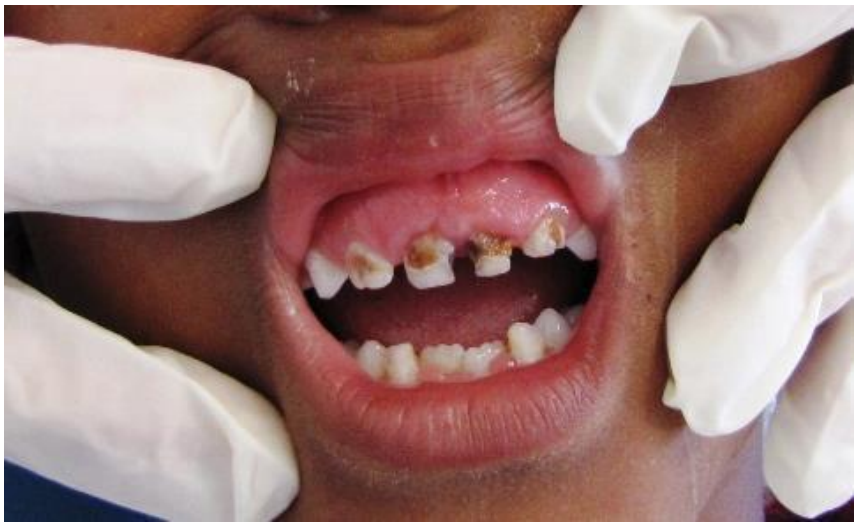


Fig 6.1 Dental caries in a girl aged 5 years with ID at a SE Facility

6.1.3 Management implications of untreated dental caries in ID

The level of co-operation of children with ID influences their dental management. Local anaesthesia is the treatment of choice for conservative management or extractions in a child who remains calm and follows instructions. However, when children are very anxious or refuse treatment, alternative methods of management warrant consideration. These approaches will be discussed in chapters 16 and 18.

6.2 Gingival Disease

The prevalence of gingival disease at the SE Facilities and the RXH was 69% and 86%, respectively. Also, the proportion of participants with gingival disease at RXH was statistically significantly higher than in 2 of the schools (Lentegeur and Blouvlei), $p < 0.05$. Chikte et al., 1990 reported similar results in a group of non-ID rural children from Transkei, as did Bamjee, Chikte & Cleaton-Jones, 1999 among institutionalized persons with ID from Gauteng, South Africa. These outcomes also follow similar trends documented in international studies that were conducted in countries within the lower-middle-income categories (Kumar et al., 2009; Altun et al., 2010; Purohit,Acharya & Bhat, 2010). The figures are, however, slightly higher than those in children with ID attending a daycare facility for children with special needs in Nigeria (Oredugba & Akindayomi, 2008).

The frequency of gingival disease was similar among males and females at both investigation sites.

The aetiology, development and progression of gingival diseases in children with ID are similar to those in non-ID children and has been well-documented (Akcalı & Lang, 2018).

The most significant causative factor of inflammatory-induced gingival disease is bacterial plaque. The inability of the participants to practice effective plaque control and to comprehend the importance of oral hygiene may explain the high prevalence of gingival disease in this study.

6.2.1 Risk factors of gingival disease in ID

The initiation and progression of gingival disease and subsequent plaque-induced periodontal disease is fundamentally determined by the host's immune response, the health of the periodontal tissues and nutritional factors. Other influences such as age and location of the

teeth within the mouth are also important determinants in the development of gingival disease (Fig 6.2). As previously mentioned, children with ID have additional risk factors that increase their susceptibility to gingival related problems. These include malnutrition, impaired immunity and defective swallowing reflexes.

Fig 6.2 A girl aged 16 years with plaque-induced gingival disease that has resulted in gingival recession and localized periodontal disease.

6.2.2.1 Malnutrition and impaired immunity

Although the precise assessment of the nutritional status of the children participating in this study was beyond the scope of the investigation, malnutrition was sometimes clinically evident. The correlation between malnutrition and infection was initially described by (Scrimshaw et al., 1968) in the mid-20th century. Malnutrition manifests in several forms and may range from clinically evident protein and carbohydrate insufficiencies to a lack of vitamins which are essential for periodontal health. Oral aversion, accompanying some forms of ID, may cause several types of dietary deficiencies. The lack of vitamins A and C are associated with defective wound healing and gingival bleeding. Similarly, a lack of vitamin D results in increased susceptibility to gingival inflammation and periodontal bone

loss (Dietrich et al., 2005; Dizdar et al., 2016). Severe malnutrition is also the predominant cause of immunosuppression worldwide (Chandra, 1997). Some genetic disorders may directly or indirectly impair the immune system and increase the risk of developing infections including periodontal disease. In the current investigation, there were several children affected by Down syndrome (DS) in which immune deficiencies is a component. Several constituents of the immune system may either be deficient or dysfunctional in children with inherited immune insufficiencies. These include T and B cell lymphopenia, a marked decrease of immature lymphocytes, impaired mitogen-induced T cell proliferation and defective of neutrophil chemotaxis. Together or individually the defects can result in a reduced response to virulent plaque bacterial strains (Ram & Chinen, 2011). Also, rapid gingival tissue destruction could be enhanced by high levels of proteolytic enzymes and inflammatory mediators in the affected children (Morgan, 2007).

6.2.2.2 Defective swallowing

During normal mastication and swallowing food, bacteria and plaque are rapidly removed from the oral cavity. Delayed or absent swallowing reflexes, which were observed during the oral investigations, result in the retention of food particles, and leading to bacteria, plaque and calculus in the mouth. Together, these processes may have contributed to the high frequency of gingival inflammation in both groups of children studied in this series.

6.2.2 Dental implications of gingival disease in ID

Similar to dental caries, gingival disease has both local and systemic complications. In this investigation, there was a positive relationship between gingival disease and missing teeth (r_s=0.423, p<0001) and dental caries at both investigation sites.

The strong correlation between gingival disease and missing teeth in the 3-8-year olds (r_s=0.680; p<0.001) compared to the weak positive relationship between the two variables in the 9-11-year old (r_s = 0.339; p =0.009) age group at the SE Facilities, suggests that apart from dental caries, gingival disease may have contributed to tooth loss in the younger participants. This relationship was not observed at the RXH.

Several factors may explain this outcome in the younger participants. As with dental caries, young children, especially those with ID, rely on their parents or caregivers to brush and floss their teeth. When parents or caregivers fail to assist children with these practices, bacteria containing plaque accumulates on teeth and may result in bleeding, swollen gums and possible premature tooth exfoliation. A thick layer of plaque on the tooth surface serves as a substrate for bacterial proliferation. If the bacterial colonies are not removed by brushing and flossing, the microbes may spread below the gingival line and release toxins that weaken the supporting tooth structure cause inflammatory-induced periodontal disease. Progressive periodontal disease may cause tooth mobility and exfoliation. The absence of the relationship between gingival disease and missing teeth at the RXH suggests additional factors may have accounted for missing teeth at this site.

A significant proportion of children in this series had malocclusion (28% at the SE Facilities and 76% at RXH). There was a positive relationship between malocclusion and gingival disease (r_s=0.25,p=0.004) at SE Facilities and in particular in the older group of

children (r_s=0.312,p=0.0134). Misplaced and crowded teeth play a crucial role in the effective removal of plaque and calculus from the dental hard tissue and serve as a nidus for the accumulation of calculus and pathogenic bacteria.

Malocclusion is discussed c o m prehensively in chapter 11.

The systemic effects of gingival disease have been well-documented (Petersen, 2003). Poor oral health and periodontal status are associated with systemic complications including diabetes (Joshipura et al., 2018), respiratory (Aida et al., 2011) and renal diseases (Akar et al., 2011). Recently, it has emerged deficient oral care may also contribute to other conditions including certain cardiovascular and hepatic disorders (Weidlich et al., 2008; Bosshardt, 2018).

Gingivitis, if not adequately managed, can progress to periodontitis, a condition which could result in pain, tooth mobility and tooth loss.

A significant proportion of the children in this series had gingival disease accompanied by mild to moderate swelling (Fig 6.3). An abnormal overgrowth of gingival tissue is referred to as gingival hypertrophy (GH) and can be categorized into four separate groups according to the aetiology viz: a) inflammatory, b) drug-induced, c) hereditary gingival fibromatosis, and d) systemic.

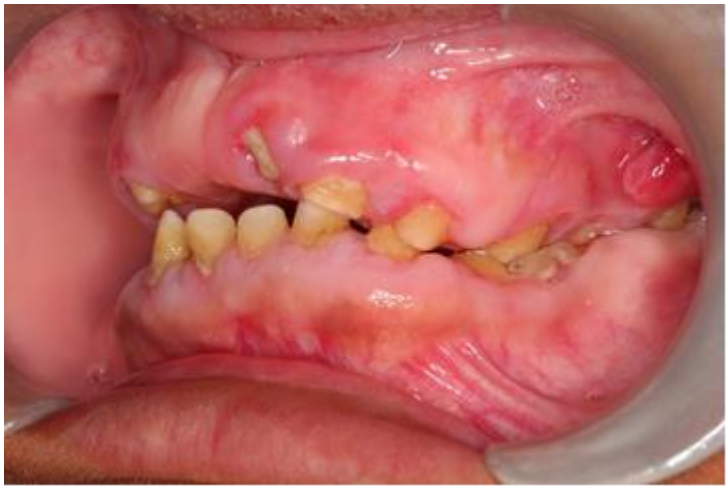


Fig 6.3 Generalized gingival hypertrophy and enamel hypoplasia (chapter 7) in a girl aged 11 years with mild ID. The aetiology of ID is currently under genetic investigation.

Inflammatory gingival hypertrophy may be localized or generalized and occurs as due to the accumulation of plaque and other irritants. In this instance, the affected gingiva is tender, soft, red, and bleeds easily (Fig 6.2). The condition resolves with the removal of plaque and irritants from the teeth.

Children with ID frequently have epilepsy and phenytoin is widely used to control epileptic seizures. The most common complication of this medicament is drug-induced gingival hypertrophy (Aragon & Burneo, 2007). Additional influences such as plaque and inflammation contribute toward the development of this disorder. Hypertension, which accompanies some genetic ID syndromes, may warrant the use of therapeutic agents such as calcium channel blockers, can also precipitate the overgrowth of gingival tissue.

The term “hereditary gingival fibromatosis” (HGF) pertains to a group of disorders that may occur in isolation or as a component of a genetic syndrome. The author’s series included

genetic ID conditions, notably Costello, Williams, Hunter and Hurler syndromes, in which excessive gingival tissue was noted .

In the Costello syndrome (Fig 6.4) GH may result from mutations in the signalling pathway of the *Ras* gene (Goodwin et al., 2014).

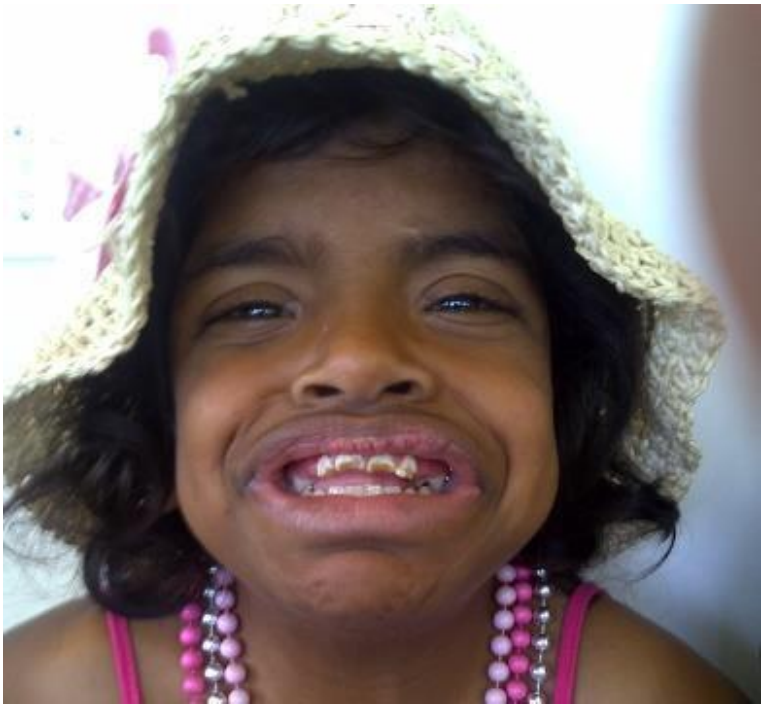


Fig 6.4 A girl aged 6 years with Costello syndrome and gingival enlargement

In the Williams syndrome, GH is likely the result of a compensatory oversecretion of collagen fibres in response to the diminished component of elastin in the gingival tissue. A possible connection between a mutation of a gene responsible for elastin secretion may be implicated in the aetiology of this disorder (Joseph et al., 2008).

Hunter and Hurler syndromes belong to a group of mucopolysaccharide disorders characterized by lysosomal enzyme defects. In these conditions deficiencies of specific enzymes result in the accumulation of glycosaminoglycans in tissues and organs including the gingiva (Gardner, 1968; Thomas & Tandon, 2000).

Apart from its local effects, gingival and periodontal diseases may influence the systemic health of susceptible individuals including those with ID. Recent research has suggested that the relationship between periodontal disease and diabetes may be reciprocative and that severe periodontal disease may perpetuate hyperglycemia in poorly controlled diabetics (Chee et al., 2013).

Children with genetic ID syndromes sometimes have structural cardiac abnormalities. These malformations, in combination with high levels of periodontal pathogens could predispose them to life-threatening infective endocarditis.

6.2.3 Management implications of gingival disease in ID

As with the general population, the primary aim in the management of gingival disease in children is to remove the aetiologic agent, provide curative treatment and establish a successful maintenance protocol. Together, these approaches prevent the recurrence and advancement of gingival disease and decrease the probability of tooth loss. However, unlike the general population, children with ID may have special considerations such as physical, intellectual and emotional challenges (chapter 12). Irrespective of the type of challenge, the primary aim of management remains the same. A sound understanding of various types of gingival disease affecting children may assist to distinguish between plaque-induced and non-plaque induced diseases and contribute in detecting underlying systemic abnormalities (Campos-Lara et al., 2012; Masamatti, Kumar & Virdi, 2012). The general management protocol includes oral health education, the control of possible risk factors such as medication, the elimination of plaque and calculus by mechanical means, the removal any defective dental restorations and plaque retentive habitats. Furthermore, adding a chemical therapeutic agent such as oral rinses reduces periodontal pathogens.

Home maintenance should be regularly followed-up for this compromised group of children.

Concluding comments:

The most common, yet avoidable, oral diseases among the participants have serious consequences that may affect their overall well-being.

Apart from the local effects documented in this chapter, namely tooth loss and malocclusion at the SE Facilities, dental caries can also impair chewing, speech and cause pain. If left untreated, tooth decay may result in deleterious ramifications. Likewise, gingival disease contributed to tooth loss among younger participants at the SE Facilities and may have compromised the systemic health of affected participants.

The correlations between dental caries and gingival disease at all investigation sites may suggest a common pathogenic pathway but highlights the importance of good oral hygiene practices.

References

1. Abanto, J., Paiva, S.M., Raggio, D.P., Celiberti, P., Aldrigui, J.M., Bönecker, M. 2012. The impact of dental caries and trauma in children on family quality of life. *Community Dentistry and Oral Epidemiology*. 40(4):323–331. doi: 10.1111/j.1600-0528.2012.00672. x.
2. Aida, J., Kondo, K., Yamamoto, T., Hirai, H., Nakade, M., Osaka, K., Sheiham, A., Tsakos, G., Watt, R.G.2011. Oral health and cancer, cardiovascular, and respiratory mortality of Japanese. *Journal of Dental Research*. 90(9): 1129–1135.
3. Akar, H., Akar, G.C., Carrero, J.J., Stenvinkel, P., Lindholm, B., 2011. Systemic consequences of poor oral health in chronic kidney disease patients. *Clinical Journal of the American Society of Nephrology.* 6(1): 218–226.
4. Akcalı, A., Lang, N.P.2018. Dental calculus: the calcified biofilm and its role in disease development. *Periodontology 2000.* 76(1): 109–115. doi.10.1111/prd.12151
5. Alaki, S. & Bakry, N. 2012. Dental Pain in Children with Intellectual Disabilities: Caregivers' Perspective. *International Journal of Dentistry*, 2012: 1-7. doi: 10.1155/2012/701608.
6. Albandar, J.M., Buischi, Y.A., Axelsson, P. 1995. Caries lesions and dental restorations as predisposing factors in the progression of periodontal diseases in adolescents. A 3-year longitudinal study. *Journal of Periodontology.* 66(4): 249–254. doi.10.1902/jop.1995.66.4.249
7. Altun, C., Guven, G., Akgun, O.M., Akkurt, M.D., Basak, F., Akbulut E. 2010. Oral health status of disabled individuals attending special schools. *European Journal of Dentistry*.4(4):361-366.
8. Anders, P.L. & Davis, E.L. 2010. Oral health of patients with intellectual disabilities: a systematic review. *Special Care in Dentistry*. 30(3):110–117. doi: 10.1111/j.1754-4505.2010.00136. x.
9. Aragon, C.E. & Burneo, J.G. 2007. Understanding the patient with epilepsy and seizures in the dental practice. *Journal of the Canadian Dental Association*. 73(1):71–76.
10. Bamjee,Y., Chikte, U. & Cleaton-Jones, P. 1999. Assessment of periodontal status and treatment needs of a disabled population using the CPITN. *South African Dental Journal*. 54(9):413–417.
11. Bosshardt, D.D.2018. The periodontal pocket: pathogenesis, histopathology and consequences. Periodontology. 2000. 76 (1) 43–50. doi: 10.1111/prd.12153.
12. Campos-Lara, P., Santos-Diaz, M., Ruiz-Rodríguez, M.S., Garrocho-Rangel, J.A., Pozos-Guillén, A.J. 2012. Orofacial findings and dental management of Williams-Beuren syndrome. *Journal of Clinical Pediatric Dentistry*. 36(4):401–404.
13. Chandra, R.1997. Nutrition and the immune system: an introduction. American *Journal of Clinical Nutrition.*66(2): 460S-463S
14. Chee, B., Park, B., Bartold, P.M., 2013. Periodontitis and type II diabetes: a two-way relationship. *International Journal of Evidence Based Healthcare*. 11(4): 317–329.
15. Chikte, U.M., Gugushe, T.S., Rudolph, M.J., Reinach, S.G. 1990. Dental caries prevalence and CPITN of 12-year-old rural schoolchildren in Transkei. *South African Dental Journa*l. 45(6):245–249.

16. Cleaton-Jones, P. & Fatti, P. 2009. Dental caries in children in South Africa and Swaziland: a systematic review 1919–2007. *International Dental Journal*. 59(6):363–368. doi: 10.1922/IDJ.
17. Cumella, S., Ransford, N., Lyons, J., Burnham, H. 2000. Needs for oral care among people with intellectual disability not in contact with Community Dental Services. *Journal of Intellectual Disability Research.* 44 (Pt 1):45–52.
18. Das, U.M., Beena, J.P. & Azher, U. 2009. Oral health status of 6- and 12-year-old school going children in Bangalore city: an epidemiological study. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 27(1):6–8. doi: 10.4103/0970-4388.50809.
19. Dellavia, C., Allievi, C., Ottolina, P., Sforza, C. 2009. Special care dentistry for people with intellectual disability in dental education: an Italian experience. *European Journal of Dental Education.* 13(4):218–222.
20. Dietrich, T., Nunn, M., Dawson-Hughes, B., Bischoff-Ferrari, H. 2005. Association between serum concentrations of 25-hydroxyvitamin D and gingival inflammation. *American Journal of Clinical Nutrition*. 82(4):575–580.
21. Disha, P., Poornima, P., Pai, S.M., Nagaveni, N.B., Roshan, N.M., Manoharan, M. 2017. Malocclusion and dental caries experience among 8-9-year-old children in a city of South Indian region: A cross-sectional survey. *Journal of Education and Health Promotion.* 6: 98.
22. Dizdar, O., Baspınar, O., Kocer, D., Dursun, Z., Avcı, D., Karakükcü, C., Çelik, İ., Gundogan, K. 2016. Nutritional risk, micronutrient status and clinical outcomes: a prospective observational study in an infectious disease clinic. *Nutrients*. 8(3):124. doi: 10.3390/nu8030124.
23. Duarte-Rodrigues, L., Ramos-Jorge, J., Drumond, C.L., Diniz, P.B., Marques, L.S., Ramos-Jorge, M.L. 2017. Correlation and comparative analysis of the CPQ8-10 and child-OIDP indexes for dental caries and malocclusion. *Brazil Oral Research.* 31, e111.
24. Fernandez, J.B., Lim, L.J., Dougherty, N., LaSasso, J., Atar, M., Daronch, M. 2012. Oral health findings in athletes with intellectual disabilities at the NYC Special Olympics. *Special Care in Dentistry.* 32(5):205–209. doi: 10.1111/j.1754-4505.2012.00268. x.
25. Gardner, D.G. 1968. Metachromatic cells in the gingiva in Hurler's syndrome. *Oral Surgery, Oral Medicine and Oral Pathology*. 26(6):782–789.
26. Goodwin, A.F., Oberoi, S., Landan, M., Charles, C., Massie, J.C., Fairley, C., Rauen, K.A., Klein, O.D. 2014. Craniofacial and dental development in Costello syndrome. *American Journal of Medical Genetics.Part A*. 164A (6):1425–1430. doi: 10.1002/ajmg.a.36475 [doi].
27. Joseph, C., Landru, M.M., Bdeoui, F., Gogly, B., Dridi, S.M. 2008. Periodontal conditions in Williams Beuren syndrome: a series of 8 cases. *European Archives of Paediatric Dentistry.* 9(3):142–147.
28. Joshipura, K.J., Muñoz-Torres, F.J., Dye, B.A., Leroux, B.G., Ramírez-Vick, M., Pérez, C.M. 2018. Longitudinal Association between Periodontitis and Development of Diabetes.*Diabetes Research and Clinical Practice.* doi: 10.1016/j.diabres.2018.04.028
29. Kirchberg, A., Treide, A. & Hemprich, A. 2004. Investigation of caries prevalence in children with cleft lip, alveolus, and palate. *Journal of Cranio-Maxillo-Facial Surgery.* 32(4):216–219. doi: 10.1016/j.jcms.2004.02.003.

30. Kumar, S., Sharma, J., Duraiswamy, P., Kulkarni, S. 2009. Determinants for oral hygiene and periodontal status among mentally disabled children and adolescents. *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 27(3):151-157. doi: 10.4103/0970-4388.57095.
31. Leroy, R., Declerck, D. & Marks, L. 2012. The oral health status of Special Olympics athletes in Belgium. *Community Dental Health*. 29(1):68–73.
32. Liu, H.Y., Chen, C.C., Hu, W.C., Tang, R.C., Chen, C.C., Tsai, C.C., Huang, S. T. 2010. The impact of dietary and tooth-brushing habits to dental caries of special school children with disability. *Research in Developmental Disabilities*. 31(6):1160–1169. doi: 10.1016/j.ridd.2010.08.005.
33. Masamatti, S., Kumar, A. & Virdi, M.S. 2012. Periodontal diseases in children and adolescents: a clinician's perspective part. *Dental Update*. 39(9):639-642.
34. Merchant, A.T., 2012. Periodontitis and dental caries occur together. *Journal of Evidence-Based Dental Practice*. 12(s3): 18–19. doi: 10.1016/S1532-3382(12)70005-2
35. Minihan, P.M., Morgan, J.P., Park, A., Yantsides, K.E., Nobles, C.J., Finkelman, M.D., Stark, P.C., Must, A.2014. At-home oral care for adults with developmental disabilities: a survey of caregivers. *Journal of American Dental Association.* 145 (10): 1018–1025.
36. Morgan, J. 2007. Why is periodontal disease more prevalent and more severe in people with Down syndrome? *Special Care in Dentistry*. 27(5):196–201. doi: 10.1111/j.1754-4505. 2007.tb00346.x.
37. Norwood, K.W. & Slayton, R.L. 2013. Oral health care for children with developmental disabilities. *American Academy of Pediatrics*.131(3):614–619. doi: 10.1542/peds.2012-3650.
38. Nqcobo, C., Yengopal, V. & Rudolf, M. 2012. Caries prevalence of children attending special needs schools in Johannesburg, Gauteng, South Africa. *South African Dental Journal*. 67(7):308–313.
39. Oredugba, F.A. & Akindayomi, Y. 2008. Oral health status and treatment needs of children and young adults attending a day centre for individuals with special health care needs. *BMC Oral Health*. 8:30. doi: 1472-6831-8-30 [pii]\n10.1186/1472-6831-8-30.
40. Petersen, P.E. 2003. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century - the approach of the WHO Global Oral Health Programme. *Community Dentistry and Oral Epidemiology*. 31(S1) 3–23.
41. Purohit, B. M., Acharya, S.& Bhat, M.2010. Oral health status and treatment needs of children attending special schools in south India: a comparative study. *Special Care in Dentistry*. 30(6):235-241. doi: 10.1111/j.1754-4505.2010.00160.x
42. Ram, G. & Chinen, J. 2011. Infections and immunodeficiency in Down syndrome. *Clinical and Experimental Immunology*. 164(1):9–16. doi: 10.1111/j.1365-2249.2011.04335. x.
43. Sá-Pinto, A.C., Rego, T.M., Marques, L.S., Martins, C.C., Ramos-Jorge, M.L., Ramos-Jorge, J. 2018. Association between malocclusion and dental caries in adolescents: a systematic review and meta-analysis. *European Archives of Paediatric Dentistry*. 19(2): 73–82.
44. Scrimshaw, N.S., Taylor, C.E. & Gordon, J.E., 1968. Interactions of nutrition and infection. *Monograph Series. World Health Organization.* 57: 3–329.

45. Shivakumar, K., Patil, S., Kadashetti, V., Raje, V. 2018. Oral Health Status and Dental Treatment Needs of 5–12-year-old Children with Disabilities Attending Special Schools in Western Maharashtra, India. *International Journal of Applied and Basic Medical Research.* 81): 24–29. doi: 10.4103/ijabmr.IJABMR_57_17
46. Smit, D.A., Barrie, R.B. & Louw, A.J. 2017. The burden of dental caries in the Western Cape and a recommended turn-around strategy. *South African Dental Journal.* 72(8):360–365.
47. Thomas, S. & Tandon, S. 2000. Hurler syndrome: a case report. *The Journal of Clinical Pediatric Dentistry*. 24(4):335–338.
48. van Wyk, P. & van Wyk, C. 2004. Oral health in South Africa. *International Dental Journal*. 54:373–377.
49. Vehkalahti, M., Paunio, I. 1994. Association between root caries occurrence and periodontal state. *Caries Research*. 28 (4):301–306. doi:10.1159/000261990
50. Weidlich, P., Cimões, R., Pannuti, C.M., Oppermann, R.V. 2008. Association between periodontal diseases and systemic diseases. *Brazilian Oral Research*. 22 (S1): 32–43.
51. Wiener, R.C. 2015. Dental Fear and Delayed Dental Care in Appalachia-West Virginia. *American Dental Hygienists Association*. 89(4): 274–281.

CHAPTER 7: DISCUSSION OF PROJECT FINDINGS: Abnormalities of tooth number

Introduction:

While the main focus of this chapter is tooth absence and for completeness, the author briefly discusses hyperdontia at the end of the chapter. The possible aetiology, dental and management implications of anomalies in tooth number are also explored.

7.1 Missing teeth

A significant proportion of the children assessed at the SE Facilities (46.5%) and the RXH (51%) had missing teeth. In general, the absence of teeth can be attributable to congenital abnormalities, the natural course of tooth eruption and exfoliation; trauma; periodontal disease and dental caries.

Cultural dental mutilation, such as extracting the maxillary central and lateral incisors are common in the local South African community and may have contributed to the high prevalence of missing teeth (Friedling & Morris, 2005; 2007) among the participants. Furthermore, the high prevalence of malocclusion in both groups of participants (30% at the SE Facilities and 76% at RXH) may also have prompted the removal of healthy teeth to "improve" aesthetics.

The relationship between missing teeth and both dental caries and gingival disease, which are more common among the younger participants, was discussed in chapter 6.

Missing teeth were more prevalent in the 9-11 year-old participants at all the investigation sites. This is not surprising since the transition from primary teeth to the permanent dentition occurs during this period ("mixed dentition").

Furthermore, there was a weak positive correlation between missing teeth and anomalies of the jaw and midface (r_s=0.17, p=0.0300) (chapter 10) at the SE Facilities. The fact that there was no association between missing teeth and any other clinical parameter at the RXH which suggests that additional factors such as hypodontia, may have contributed to the high prevalence of missing teeth at this investigation site.

7.1.1 Hypodontia

Traditionally, hypodontia refers to the congenital absence of one to six teeth (Fig 7.1). When more than six teeth fail to develop the term "oligodontia" is preferred. The complete congenital absence of teeth is called "anodontia" (Wang et al., 2016) . The global prevalence of hypodontia is 6.4%, with African populations experiencing the greatest risk for tooth agenesis (13.4%) (Khalaf et al., 2014).

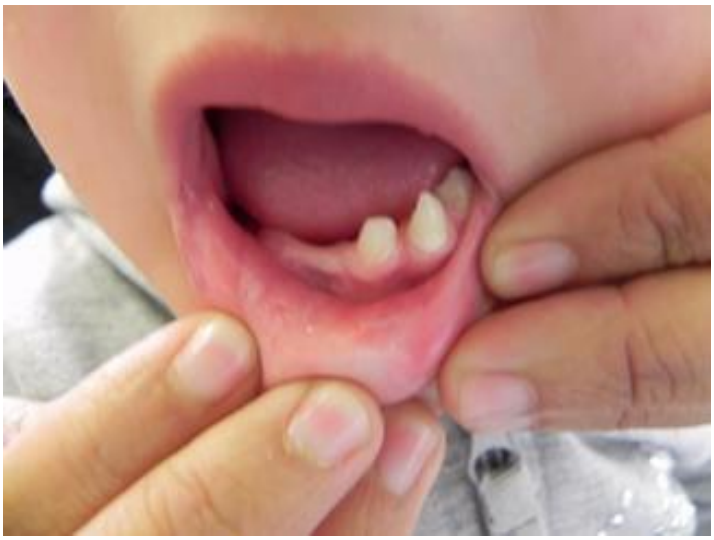


Fig 7.1 Hypodontia in a girl aged 4 years with Incontinentia pigmenti.

The prevalence of the congenital absence of teeth in the general ID population has not been documented. Isolated studies have reported the prevalence of hypodontia in individual genetic ID syndromes to vary from between 38.6% and 68% (Mestrovic, Rajic & Papic, 1998; Suri, Tompson & Atenafu, 2011).

Hypodontia is more common in the permanent dentition and is either symmetrical or occurs haphazardly. The absence of deciduous teeth is uncommon, but when this occurs the successive permanent tooth usually fails to develop. Mutations in *PAX 9* and *MSX 1* genes are associated with autosomal dominant inheritance absence of posterior teeth. Mutations in the *AXIN2* gene are related to non-syndromic hypodontia (Wang et al., 2016). In addition, recent studies have supported the role of genetic, epigenetic and environmental influences in tooth agenesis (Abdalla et al., 2014). The genetic ID syndromes associated with hypodontia encountered during the investigation are tabulated in Table VII.1

Table VII.1: Genetic ID syndromes associated with hypodontia

Syndrome	Reference
Apert	De Coster et al., 2009
Coffin-Lowry	Hanauer & Young, 2002; Wasersprung & Sarnat, 2006
Down	Mestrovic, Rajic & Papic, 1998; De Coster et al., 2009; Suri, Tompson & Atenafu, 2011; van Marrewijk et al., 2016
Kabuki	Seymen, Tuna & Kayserili, 2002; Teixeira et al., 2009; Sobral et al., 2013
Rubeinstein-Taybi	Hennekam & Van Doorne, 1990
Seckel	Regen, Nelson & Woo, 2010
Sotos	Hirai, Matsune & Ohashi, 2011
Williams	Hertzberg et al., 1994; Axelsson et al., 2003; Mass, Oelgiesser & Tal, 2007; Ramachandra, Singh & Wong, 2015
Wolf-Hirschhorn	Johnston & Franklin, 2006

Environmental influences such as anticancer therapies, certain infections, as well as genetic mutational changes during any stage of morphogenesis can influence or impede tooth development.

7.1.2 Dental implications of missing teeth/ hypodontia in ID

The absence of one or more teeth can result in various problems such as challenges with speech and mastication. In due course, the remaining teeth will drift into spaces left behind by the missing teeth. Apart from forming food and plaque traps (chapter 6), the drifted teeth may cause malocclusion (chapter 8) and eventually result in pain and dysfunction of the temporomandibular joint.

The strength and integrity of the alveolar bone depends on vibration and pressure exerted by tooth contact. When teeth are lost, the bone no longer receives the stimulation which is necessary for the maintainance of its shape and density resorbtion begins.

7.1.3 Dental management implications of hypodontia/missing teeth in ID

Improving the aesthetics of children with ID by replacing missing teeth improves their mental health and subsequently their general well-being (Aroon, 1989). Although there are several intervention strategies for replacing extracted or congenitally absent teeth, none of the children in this study had any prosthetic rehabilitation. While numerous factors determine the success of replacing missing teeth in children with ID, the protocol is the same as in non-ID individuals. Oral habits such as bruxism, tongue thrust and thumb-sucking need to be considered when planning treatment. Additional considerations such as the presence or absence of malocclusion and the jaw relationships are determining factors in choosing appropriate management regimes. The most cost-effective means for improving aesthetics and function in children with ID is the provision of removable dentures. Before implementing an intervention strategy, a needs analysis could assist in the adjustment and compliance of wearing these appliances.

The ingestion and aspiration of removable dentures sometimes occur occurs in children and persons with ID. In addition, some children with ID are prone to exhibit aggressive behaviour and may use the denture as a tool for mutilation.

Children with congenitally missing teeth often have structural tooth abnormalities (chapter 8) and prior reconstruction of dental hard tissue may be required. In these instances, multiple procedures across different disciplines of dentistry will be necessary. Despite the fact permanent prostheses pose less risks, they are extremely costly. Moreover, the

maintenance of dental implants, crowns and bridges requires meticulous oral hygiene. In this study, the high frequency of gingival disease and poor oral hygiene precluded the aforementioned procedures in the majority of the children.

7.2 Hyperdontia

Although none of the children in this study had visible supernumerary teeth it is relevant that supernumerary teeth may not be visible in the mouth and their presence is often established by radiographic techniques (Fig 7.2).

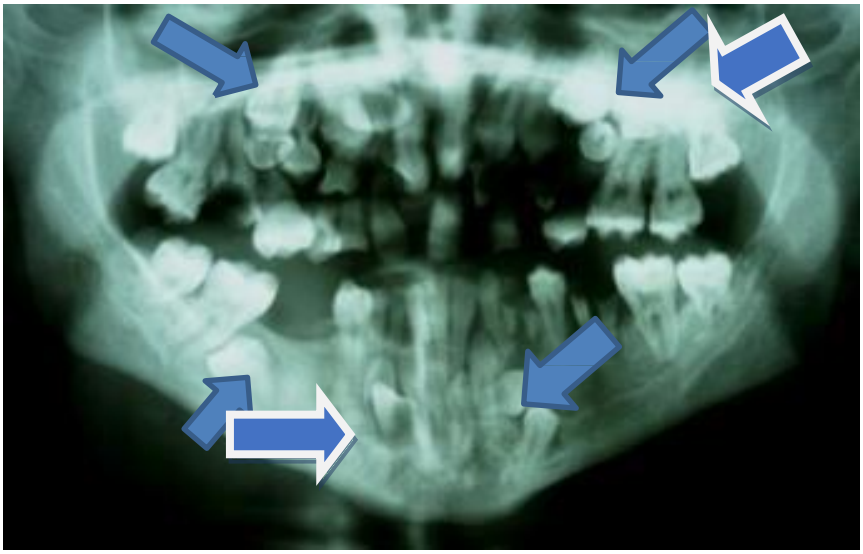


Fig 7.2 Multiple unerupted supernumerary teeth detected on orthopantamogram (blue arrows)

Supernumerary teeth (ST) are common in both jaws. An extra tooth found between the maxillary central incisors, termed "mesiodens", is the most commonly occurring surplus tooth. Supernumerary teeth may bear a resemblance to normal teeth (supplemental teeth) or have distorted morphologies with conical crowns and short roots (accessory ST).

Hyperdontia can occur in isolation or as a component of specific genetic ID syndromes including Rubinstein-Taybi syndrome and Trico–Rhino–Phalangeal syndrome. Although the exact pathogenic mechanism of ST is unknown, it may result from hyperactivity of tooth buds or a mutation of the *Cbfa 1* and *RUNX-2* genes (Martins, de Souza & Giovani, 2014). The *RUNX-2* gene plays an important role in the epithelial-mesenchymal interfaces that regulate progressive embryonic tooth development and histodifferentiation of the epithelial enamel

organ and in this way has an inhibitory effect on the tooth bud formation. Some mutated forms of the gene lack its normal inhibitory function, resulting in excessive tooth germ development (Subasioglu et al., 2015).

Concluding comments:

Anomalies of tooth number play a significant role in the day to day function of the persons affected by ID. Although restoring function and aesthetics is possible, it is more than often complicated and require the involvement of a multidisciplinary dental team.

References:

1. Abdalla E, Mostowska A, Jagodziński P, Dwidar K, I.S. 2014. A novel *WNT10A* mutation causes non-syndromic hypodontia in an Egyptian family. *Archives of Oral Biology*. 59(7):722–728. doi: 10.1016/j.archoralbio.2014.04.004.
2. Aroon, S. 1989. Social and psychological improvement of two handicapped patients by oral rehabilitation. *Journal of the Dental Association of Thailand*. 39(6):209–18.
3. Axelsson, S., Bjornland, T., Kjaer, I., Heiberg, A., Storhaug, K. 2003. Dental characteristics in Williams syndrome: a clinical and radiographic evaluation. *Acta Odontologica Scandinavica*. 61(3):129–136.
4. De Coster, P.J., Marks, L.A., Martens, L.C., Huysseune, A. 2009. Dental agenesis: genetic and clinical perspectives. *Journal of Oral Pathology and Medicine*. 38(1):1–17. doi:10.1111/j.1600-0714.2008.00699. x.
5. Friedling, L.J. & Morris, A.G. 2005. The frequency of culturally derived dental modification practices on the Cape flats in The Western Cape. *South African Dental Journal*. 60(3):97, 99–102.
6. Friedling, L.J. & Morris, A.G. 2007. Pulling teeth for fashion: dental modification in modern day Cape Town, South Africa. *South African Dental Journal*. 62(3):106, 108–13.
7. Hanauer, A. & Young, I. 2002. Coffin-Lowry syndrome: clinical and molecular features. *Journal of Medical Genetics*. 77(10):705–713. doi:10.1136/jmg.39.10.705.
8. Hennekam, R.C. & Van Doorne, J.M. 1990. Oral aspects of Rubinstein-Taybi syndrome. *American Journal of Medical Genetics.* 37(Suppl 6):42–47.
9. Hertzberg, J., Nakisbendi, L., Needleman, H.L., Pober, B. 1994. Williams syndrome--oral presentation of 45 cases. *Pediatric Dentistry*. 16(4):262–267.
10. Hirai, N., Matsune, K. & Ohashi, H. 2011. Craniofacial and oral features of Sotos syndrome: differences in patients with submicroscopic deletion and mutation of *NSD1* gene. *American Journal of Medical Genetics.Part A*. 155(12):2933–2939. doi:10.1002/ajmg.a.33969.
11. Johnston, N.J. & Franklin, D.L. 2006. Dental findings of a child with Wolf-Hirschhorn syndrome. *International Journal of Paediatric Dentistry.* 16(2):139–42.doi:10.1111/j.1365-263x.2006.00675. x.
12. Khalaf, K., Miskelly, J., Voge, E., Macfarlane, T. V. 2014. Prevalence of hypodontia and associated factors: a systematic review and meta-analysis. *Journal of Orthodontics*. 41(4):299–316. doi:10.1179/1465313314y.0000000116.
13. Martins, R.B., de Souza, R.S. & Giovani, E.M. 2014. Cleidocranial dysplasia: report of six clinical cases. *Special Care in Dentistry*. 34(3):144–150. doi:10.1111/scd.12045.
14. Mass, E., Oelgiesser, D. & Tal, H. 2007. Transitional implants in a patient with Williams-Beuren syndrome: a four-year follow-up. *Special Care in Dentistry.* 27(3):112–116.

15. Mestrovic, S.R., Rajic, Z. & Papic, J.S. 1998. Hypodontia in patients with Down's syndrome. *Collegium Antropologicum.* 22 (Suppl):69–72.

16. Ramachandra, S., Singh, A. & Wong, D. 2015. Dental management of patient with Williams syndrome - a case Report. *Contemporary Clinical Dentistry*. 6(3):418-420. doi:10.4103/0976-237x.161908.

17. Regen, A., Nelson, L.P. & Woo, S.B. 2010. Dental manifestations associated with Seckel syndrome type II: a case report. *Pediatric Dentistry*. 32(5):445–450.

18. Seymen, F., Tuna, B. & Kayserili, H. 2002. Seckel syndrome: report of a case. *Journal of Clinical Pediatric Dentistry*. 26(3):305–309.

19. Sobral, S.D.P., Leite, A.F., Figueiredo, P.T.S., Ferrari, I., Safatle, H.P.N., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013. Craniofacial and dental features in Kabuki syndrome patients. *Cleft Palate-craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.

20. Subasioglu, A., Savas, S., Kucukyilmaz, E., Kesim, S., Yagci, A., Dundar, M. 2015. Genetic background of supernumerary teeth. *European Journal of Dentistry*. 9(1):153–158. doi:10.4103/1305-7456.149670.

21. Suri, S., Tompson, B.D. & Atenafu, E. 2011. Prevalence and patterns of permanent tooth agenesis in Down syndrome and their association with craniofacial morphology. *Angle Orthodontist*. 81(2):260–269. doi:10.2319/070910-391.1.

22. Teixeira, C.S., Silva, C.R., Honjo, R.S., Bertola, D.R., Albano, L.M., Kim, C.A. 2009. Dental evaluation of Kabuki syndrome patients. *Cleft Palate-craniofacial Journal*. 46(6):668–673. doi:10.1597/08-077.1

23. van Marrewijk, D.J.F., van Stiphout, M.A.E., Reuland-Bosma, W., Bronkhorst, E.M., Ongkosuwito, E.M. 2016. The relationship between craniofacial development and hypodontia in patients with Down syndrome. *European Journal of Orthodontics*. 38(2):178–183. doi:10.1093/ejo/cjv054.

24. Wang, J., Sun, K., Shen, Y., Xu, Y., Xie, J., Huang, R., Zhang, Y., Xu, C., et al. 2016. DNA methylation is critical for tooth agenesis: implications for sporadic non-syndromic anodontia and hypodontia. *Scientific Reports*. 6(301):19162. doi:10.1038/srep19162.

25. Wasersprung, D. & Sarnat, H. 2006. Coffin-Lowry syndrome: findings and dental treatment. *Special Care in Dentistry*. 26(5):220–224. doi:10.1111/j.1754-4505. 2006.tb01442. x.

CHAPTER 8: DISTURBANCES OF TOOTH SIZE

In the context of this thesis, the author has included several types of morphological tooth anomalies under the broader heading of "structural abnormalities of teeth". These only pertain clinically evident variations and changes detected by radiographic and histological techniques were excluded from this component of the study.

Chapters 8 and 9 discusses the various structural anomalies of teeth. The author deemed it necessary to include 2 separate chapters in the thesis because of the volume of the topic's content. Chapter 8 focuses on the disturbances in tooth size and chapter 9 on changes in enamel and dentine. Eleven participants (7%) at the SE Facilities and 19 participants (38%) at RXH had one of more anomalies of tooth structure. The proportion of participants with structural tooth abnormalities at RXH was statistically significantly higher in comparison with the SE Facilities sites, $p < 0.05$.

8.1 Macrodontia

Any tooth which appears to be larger than normal is termed a "macrodont" (Fig 8.1). True macrodontia involving the entire dentition is rare and may be the result of a disturbance of morphodifferentiation. Pseudo-macrodontia occurs when the jaws are smaller relative to the normal size of the teeth.

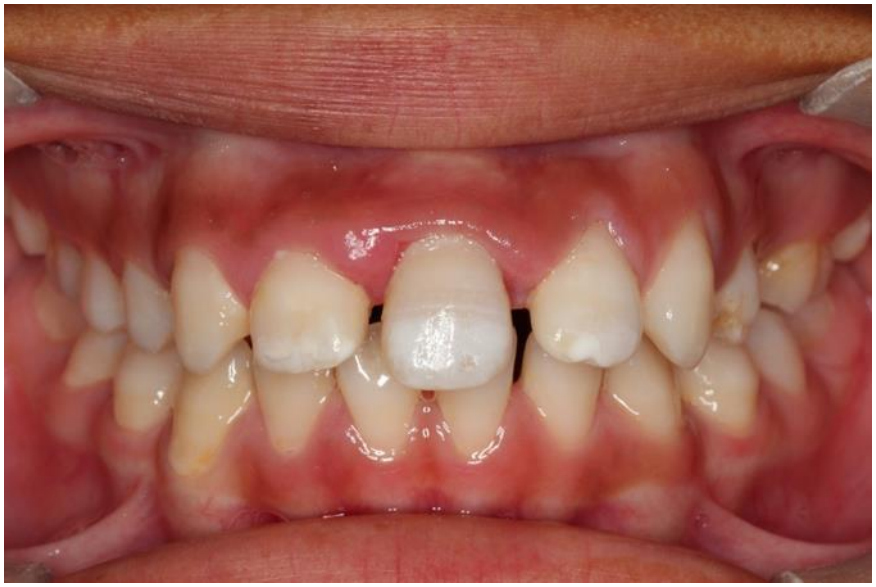


Fig 8.1 A boy aged 13 years with a single enlarged central incisor

8.2 Microdontia

Microdontia (Fig 8.2) is a developmental anomaly that can affect either the deciduous or the permanent teeth. It may either accompany genetic ID syndromes (Table VIII.1) or occur in non- genetic disorders such as a complication of radiation or chemotherapy therapy. The condition may also accompany hypodontia (chapter 7).

Table VIII.1: Genetic syndromes associated with microdontia documented in the survey

Syndrome	Reference
Bardet-Biedl	Drugowick et al., 2007; Majumdar et al., 2012; Ferreira do Amaral et al., 2014
Coffin-Lowry	Norderyd & Aronsson, 2012
Costello	Takahashi & Ohashi, 2013
Hurler	McGovern et al., 2010
Incontinentia Pigmenti	Welbury & Welbury, 1999; Macey-Dare & Goodman, 1999; Doruk, Bicakci & Babacan, 2003
Kabuki	Matsune et al., 2001; Cogulu et al., 2008; Teixeira et al., 2009; Tuna et al., 2012; Sobral et al., 2013
Oculodentodigital Dysplasia	Tumminelli et al., 2015; Doshi et al., 2016
Seckel	Seymen, Tuna & Kayserili, 2002; De Coster et al., 2006;De Coster et al., 2009
Sotos	De Coster et al., 2009; Hirai, Matsune & Ohashi, 2011
Williams	Hertzberg et al., 1994; Axelsson et al., 2003; Moskovitz et al., 2005; De Coster et al., 2009; Torres et al., 2015
Wolf-Hirschhorn	Johnston and Franklin, 2006

Shafer, Hine & Levy (1983) classified microdontia into three categories viz:

a. True generalized microdontia in which all the teeth are smaller than normal.

b. Relative generalized microdontia occur where the jaws are smaller than average but teeth are normal in size

c. Microdontia of one tooth.

Microdontia of a single tooth can be subclassified into 3 types (Ufomata, 1988):

1. Microdontia of the entire tooth
2. Microdontia of only the crown
3. Microdontia involving only the root

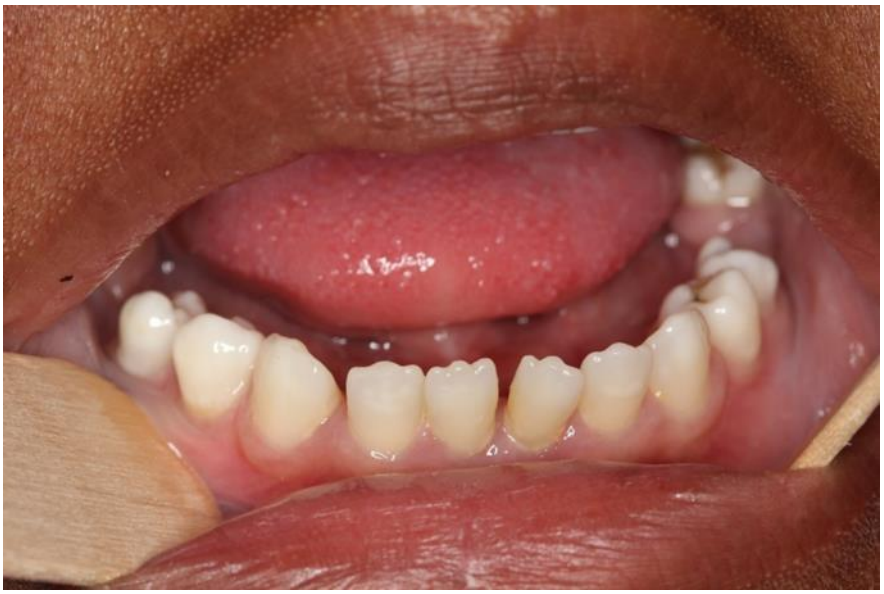


Fig 8.2 A girl aged 11 years with the CANDLE syndrome who presented with microdontia at the RXH

8.2.1 The genetics of microdontia

More than 300 genes are thought to be linked with tooth formation (Galluccio, Castellano & La Monaca, 2012). Several of these genes control the ectodermal-mesenchymal interactions which are required to form teeth in a predetermined sequence. Subsequently, these regulate the morphology, quantity and dimensions of teeth. Comparable interactions occur during general fetal development and often involve identical genes. Hence, the presence of dental abnormalities in genetic syndromes may serve as signs of common growth-related influences in dental and other tissues (Brook, 2009).

The association between general development and tooth dimension signifies that constant ectodermal–mesenchymal interaction takes place at the commencement of tooth development and continues during tooth morphogenesis. While epigenetic factors govern the location of the odontogenic tissue in the jaw, encoding of the connecting signals regulate differences in tooth size (chapter 9).

8.2.2 Dental management implications of microdontia in ID

The dental management of microdontia in ID is aimed mainly at restoration of function and aesthetics. The general management protocols are followed with special consideration to the challenges faced by children with ID (chapter 12 and chapter 13).

References

1. Axelsson, S., Bjornland, T., Kjaer, I., Heiberg, A. & Storhaug, K. 2003. Dental characteristics in Williams syndrome: a clinical and radiographic evaluation. *Acta Odontologica Scandinavica*. 61(3):129–136.
2. Brook, A.H. 2009. Multilevel complex interactions between genetic, epigenetic and environmental factors in the aetiology of anomalies of dental development. *Archives of Oral Biology*. 54(Suppl 1):3-17. doi: 10.1016/j.archoralbio.2009.09.005.
3. Cogulu, D., Oncag, O., Celen, E., Ozkinay, F. 2008. Kabuki syndrome with additional dental findings: a case report. *Journal of Dentistry for Children*. 75(2):185–187.
4. De Coster, P.J., Verbeeck, R.M.H., Holthaus, V., Martens, L.C., Vral, A. 2006. Seckel syndrome associated with oligodontia, microdontia, enamel hypoplasia, delayed eruption, and dentin dysmineralization: a new variant? *Journal of Oral Pathology & Medicine.* 35(10):639–641. doi:10.1111/j.1600-0714.2006.00462. x.
5. De Coster, P.J., Marks, L.A., Martens, L.C., Huysseune, A. 2009. Dental agenesis: Genetic and clinical perspectives. *Journal of Oral Pathology and Medicine*. 38(1):1–17. doi:10.1111/j.1600-0714.2008.00699. x.
6. Doruk, C., Bicakci, A.A. & Babacan, H. 2003. Orthodontic and orthopedic treatment of a patient with Incontinentia pigmenti. *Angle Orthodontist*. 73(6):763–768. doi:10.1043/0003-3219(2003)073<0763: OAOTOA>2.0. co.2
7. Doshi, D.C., Limdi, P.K., Parekh, N. V., Gohil, N.R. 2016. Oculodentodigital dysplasia. *Indian Journal of Ophthalmology*. 64(3):227–230. doi:10.4103/0301-4738.180191.
8. Drugowick, R.M., Da Rós Gonçalves, L., Barrôso, A.S., Feres-Filho, E.J., Maia, L.C. 2007. Treatment of gingival overgrowth in a child with Bardet-Biedl syndrome. *Journal of Periodontology*. 78(6):1159–1163. doi:10.1902/jop.2007.060378.
9. Ferreira do Amaral, C.O., Logar, G.D.A., Parisi, A.G., Takahashi, K., Straioto, F.G. 2014. General and stomatologic aspects of Bardet-Biedl syndrome. *Journal of Craniofacial Surgery*. 25(6):e575–e578. doi:10.1097/scs.0000000000001169.
10. Galluccio, G., Castellano, M. & La Monaca, C. 2012. Genetic basis of non-syndromic anomalies of human tooth number. *Archives of Oral Biology*. 57(7):918–930. doi: 10.1016/j.archoralbio.2012.01.005.
11. Hertzberg, J., Nakisbendi, L., Needleman, H.L., Pober, B. 1994. Williams syndrome--oral presentation of 45 cases. *Pediatric Dentistry*. 16(4):262–267.
12. Hirai, N., Matsune, K. & Ohashi, H. 2011. Craniofacial and oral features of Sotos syndrome: differences in patients with submicroscopic deletion and mutation of *NSD1* gene. *American Journal of Medical Genetics.Part A*. 155(12):2933–2939. doi:10.1002/ajmg.a.33969
13. Johnston, N.J. & Franklin, D.L. 2006. Dental findings of a child with Wolf-Hirschhorn syndrome. *International Journal of Paediatric Dentistry*. 16(2):139–142. doi:10.1111/j.1365-263x.2006.00675.x.
14. Macey-Dare, L. V. & Goodman, J.R. 1999. Incontinentia pigmenti: seven cases with dental manifestations. *International Journal of Paediatric Dentistry.* 9(4):293–297.
15. Majumdar, U., Arya, G., Singh, S., Pillai, A., Nair, P.P. 2012. Oro-dental findings in Bardet-Biedl syndrome. *Case Reports*. (apr23 1): bcr1220115320-bcr1220115320. doi:10.1136/bcr.12.2011.5320.

16. Matsune, K., Shimizu, T., Tohma, T., Asada, Y., Ohashi, H., Maeda, T. 2001. Craniofacial and dental characteristics of Kabuki syndrome. *American Journal of Medical Genetics*. 98(2):185–190.
17. McGovern, E., Owens, L., Nunn, J., Bolas, A., Meara, A.O., Fleming, P. 2010. Oral features and dental health in Hurler syndrome following hematopoietic stem cell transplantation. *International Journal of Paediatric Dentistry*. 20(5):322–329. doi:10.1111/j.1365-263x.2010.01055. x.
18. Moskovitz, M., Brener, D., Faibis, S., Peretz, B. 2005. Medical considerations in dental treatment of children with Williams syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 99(5):573–580. 10.1016/j.tripleo.2004.03.019
19. Norderyd, J. & Aronsson, J. 2012. Hypoplastic root cementum and premature loss of primary teeth in Coffin-Lowry syndrome: a case report. *International Journal of Paediatric Dentistry.* 22(2):154–156. doi:10.1111/j.1365-263x.2011.01160. x.
20. Seymen, F., Tuna, B. & Kayserili, H. 2002. Seckel syndrome: report of a case. *Journal of Clinical Pediatric Dentistry*. 26(3):305–309.
21. Shafer, W.G., Hine, M.K., & Levy, B.M. 1983. Develpmental Disturbances of oral and paraoral structures. In *A Textbook of Oral Pathology*.4th ed. Philadelphia: W. B. Saunders Co. p37.
22. Sirmaci, A., Spiliopoulos, M., Brancati, F., Powell, E., Duman, D., Abrams, A., Bademci, G., Agolini, E. et al. 2011. Mutations in *ANKRD11* cause KBG syndrome, characterized by intellectual disability, skeletal malformations, and macrodontia. *American Journal of Human Genetics*. 89(2):289–294. doi: 10.1016/j.ajhg.2011.06.007.
23. Sobral, S.D.P., Leite, A.F., Figueiredo, P.T.S., Ferrari, I., Safatle, H.P.N., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013. Craniofacial and dental features in Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.
24. Takahashi, M. & Ohashi, H. 2013. Craniofacial and dental malformations in Costello syndrome: A detailed evaluation using multi-detector row computed tomography. *Congenital Anomalies*. 53(2):67–72. doi:10.1111/cga.12004.
25. Teixeira, C.S., Silva, C.R., Honjo, R.S., Bertola, D.R., Albano, L.M., Kim, C.A. 2009. Dental evaluation of Kabuki syndrome patients. *The Cleft Palate-Craniofacial Journal*. 46(6):668–673. doi:10.1597/08-077.1.
26. Torres, C.P., Valadares, G., Martins, M.I., Borsatto, M.C., Diaz-Serrano, K. V., Queiroz, A.M. 2015. Oral findings and dental treatment in a child with Williams-Beuren syndrome. *Brazilian Dental Journal*. 26(3):312–316. doi:10.1590/0103-6440201300335.
27. Tumminelli, G., Di Donato, I., Guida, V., Rufa, A., De Luca, A., Federico, A. 2015. Oculodentodigital dysplasia with massive brain calcification and a new mutation of *GJA1* gene. *Journal of Alzheimer's Disease*. 49(1):27–30. doi:10.3233/jad-150424.
28. Tuna, E.B., Marşan, G., Gençay, K., Seymen, F. 2012. Craniofacial and dental characteristics of Kabuki syndrome: nine years cephalometric follow-up. *Journal of Clinical Pediatric Dentistry*. 36(4):393–400.
29. Ufomata D. 1988. Microdontia of a mandibular second premolar. *Oral Surgery, Oral Medicine, Oral Pathology*. 65(5):637–638.
30. Welbury, T.A. & Welbury, R.R. 1999. Incontinentia pigmenti (Bloch-Sulzberger syndrome): report of case. *ASDC Journal of Dentistry for Children*. 66(3):213–5, 155.

CHAPTER 9: STRUCTURAL ABNORMALITIES OF TEETH – ENAMEL AND DENTINE

Introduction

Disturbances in the components of the primary teeth are rare, and if they do occur, they predominantly manifest as tooth discoloration. The aetiology may include metabolic derangements, congenital syphilis, the maternal use of tetracycline during pregnancy and low birth weight (Ferrini, Marba & Gavião, 2008). They may also be associated with heritable disorders such as hypophosphatemic rickets (Abe et al., 1988) .

9.1 Disturbances of Enamel

9.1.1 Amelogenesis Imperfecta (AI)

Amelogenesis Imperfecta is a heritable developmental disturbance of enamel which usually occurs independent of additional systemic conditions. The disorder can be inherited as autosomal dominant, recessive or X-linked traits. Genes implicated in the aetiology include *AMELX, ENAM, MMP-20, KLK4, DLX3, Ambnchan* (Chan et al., 2011).

Regardless of its genetic basis, the general clinical features of different forms of genetic AI are similar.

The classification of AI is both variable and complex; the most widely used system was proposed by Witkop (1988) and based on the clinical appearance of the enamel and its inheritance pattern.

A diagnosis of AI is established on a family history, oral radiographs, and where available, pedigree data. Molecular genetic testing to confirm a diagnosis and determine the mode of inheritance may also be performed.

Dental implications of AI in ID

The condition may affect any number of teeth of both dentitions, vary in colour from yellow to brown or grey and have an increased risk for dental caries. In addition, they are hypersensitive to changes in temperature, and prone to early and rapid attrition.

9.1.2 Enamel Hypoplasia

In the context of the author's study, diagnostic testing to confirm AI was not available. For this reason, enamel lesions resembling AI were classified by the author as "enamel hypoplasia" (Fig 9.1). Enamel hypoplasia is more common in the primary teeth than in the permanent teeth of children with ID (Bhat & Nelson, 1989). The genetic ID syndromes associated with enamel hypoplasia encountered during the investigation are tabulated Table IX.1.

Table IX.1: Genetic ID syndromes associated with enamel hypoplasia

Syndrome	**Reference**
Kabuki	Matsune et al., 2001; Spano et al., 2008; Teixeira et al., 2009; Sobral et al., 2013
Oculo-dento-digital Dysplasia	Aminabadi et al., 2009; Aminabadi et al., 2010; Doshi et al., 2016
Prader-Willi	Foster 1971; Bazopoulou-Kyrkanidou & Papagiannoulis, 1992; Scardina, Fuca & Messina, 2007
Rubeinstein-Taybi	Seymen, Tuna & Kayserili, 2002
Seckel	Bloch-Zupan et al., 2007; Regen, Nelson & Woo, 2010
Sotos	Inokuchi et al., 2001; Gomes-silva et al., 2006; Hirai,Matsune & Ohashi, 2011
Williams	Torres et al., 2015; Wong, Ramachandra & Singh, 2015

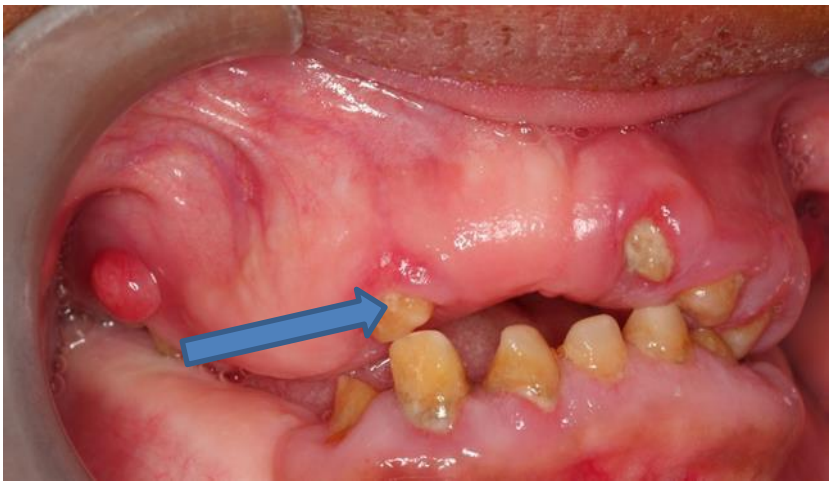


Fig 9.1 Enamel hypoplasia in a girl aged 11 years with mild ID. The aetiology of the ID is currently under genetic investigation. Generalized gingival hypertrophy is also present (chapter 6)

9.1.3 Congenital Syphilis

In recent years there has been a worldwide escalation in the prevalence of syphilis and a consequential increase in the morbidity and mortality of congenital syphilis. In the context of this thesis, the medical histories of the majority of children partaking in the study were unavailable to the author. For this reason, the prevalence of congenital syphilis was unknown and morphological alterations in the teeth were included in the category of structural tooth abnormalities. Although only 30% of individuals affected by congenital syphilis have dental changes, it is important to recognise their manifestations. From a dental perspective, syphilis affects the structure of the incisor and molar teeth. While the morphological features of the dental alterations are characteristic; they may present as a spectrum. The classical clinical features of the incisors, termed either “Hutchinson’s teeth” or “screwdriver incisors”, include small central maxillary teeth with a curved notch along the incisal edge. The size of the notch varies from being barely noticeable to a broad, crescent-shaped loss of enamel.

There are two morphological variants of the molars accompanying congenital syphilis viz Moon’s molars and Fournier’s molars, both of which affect the first permanent molars.

Moon's molars are small and curved while Fournier's molars have small, crowded cusps (Ioannou et al., 2016). Both morphological types have been referred to as "mulberry molars" as they resemble mulberry fruit (Karnosh, 1926). As previously mentioned, in the investigation, the medical background of some children was not available to the examiner. Although the clinical appearances of teeth in these children sometimes resembled those caused by congenital syphilis, in the circumstances, it was not appropriate to assume that this condition was necessarily the cause.

9.2 Disturbances of Dentine

9.2.1 Dentinogenesis Imperfecta (DI)

Dentinogenesis Imperfecta is an inherited developmental disturbance of dentine. Non-syndromic DI is caused by mutation of *DSPP* genes and represents a single disorder with variable clinical expression (Bai et al., 2010). The condition can affect all teeth in both deciduous and permanent dentitions. Affected teeth are translucent and blue to brown in colour (Fig 9.2).

In the pathogenesis of DI it is relevant that the enamel and dentine are easily separate from each other. Once the enamel is chipped away, the exposed dentine shows accelerated attrition. Isolated instances of DI associated with ID have been reported in the literature (Cauwels et al., 2005; Aminabadi et al., 2009).

Osteogenesis Imperfecta (OI), an inherited bone disorder, which may be associated with dental changes. Dentinogenesis imperfecta associated with OI is encountered worldwide in the autosomal dominant varieties of OI with mutations in the *COL1A1/COL1A2* genes. Mutations in *CRTAP, FKBP10, LEPRE1, PLOD2, PPIB, SERPINF1, SERPINH1, SP7, WNT1, BMP1, and TMEM38B* genes are causative in less common autosomal recessive forms of OI (Valadares

et al., 2014). In South Africa, mutations in the *FKBP10* gene is have been isolated in OI type 3 among indigenous black persons (Vorster et al., 2017).

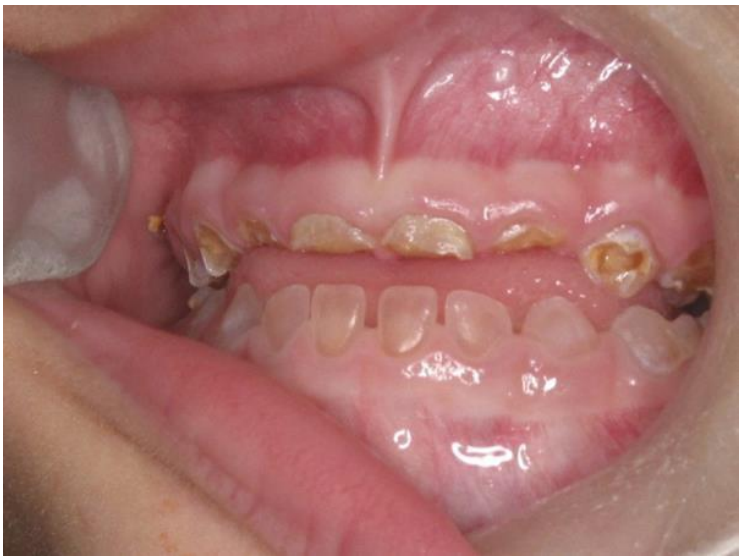


Fig 9.2 A girl aged 5 years with dentinogenesis imperfecta of her of the primary teeth and ID of unknown aetiology.

9.3 Management implications of structural tooth abnormalities in ID

The management of structural tooth abnormalities in children with ID has the aim of providing optimal function and aesthetics. The treatment protocols are usually individualized and may extend over long periods of time. Apart from the dental, occlusal and skeletal challenges related to these disorders, factors associated with ID require consideration.

References

1. Abe, K., Ooshima, T., Lily, T.S., Yasufuku, Y., Sobue, S. 1988. Structural deformities of deciduous teeth in patients with hypophosphatemic vitamin D-resistant rickets. *Oral Surgery, Oral Medicine, and Oral Pathology*. 65(2):191–198.

2. Aminabadi, N.A., Ganji, A.T., Vafaei, A., Pourkazemi, M., Oskouei, S.G. 2009. Oculodentodigital dysplasia: disease spectrum in an eight-year-old boy, his parents and a sibling. *Journal of Clinical Pediatric Dentistry*. 33(4):337–341.

3. Aminabadi, N.A., Pourkazemi, M., Oskouei, S.G. & Jamali, Z. 2010. Dental management of Oculodentodigital dysplasia: a case report. *Journal of Oral Science*. 52(2):337–342. doi: jst. jstage/josnusd/52.337.

4. Bai, H., Agula, H., Wu, Q., Zhou, W., Sun, Y., Qi, Y., Latu, S., Chen, Y., et al. 2010. A novel *DSPP* mutation causes dentinogenesis imperfecta type II in a large mongolian family. *BMC Medical Genetics*. 11:23. doi:10.1186/1471-2350-11-23.

5. Bazopoulou-Kyrkanidou, E. & Papagiannoulis, L. 1992. Prader-Willi syndrome: report of a case with special emphasis on oral problems. *Journal of Clinical Pediatric Dentistry*. 17(1):37–40.

6. Bhat, M. & Nelson, K.B. 1989. Developmental enamel defects in primary teeth in children with cerebral palsy, mental retardation, or hearing defects: a review. *Advances in Dental Research*. 3(2):132–142.

7. Bloch-Zupan, A., Stachtou, J., Emmanouil, D., Arveiler, B., Griffiths, D., Lacombe, D. 2007. Oro-dental features as useful diagnostic tool in Rubinstein-Taybi syndrome. *American Journal of Medical Genetics. Part A*. 143(6):570–573. doi:10.1002/ajmg.a.31622.

8. Cauwels, R.G.E.C., De Coster, P.J., Mortier, G.R., Marks, L.A.M., Martens, L.C. 2005. Dentinogenesis imperfecta associated with short stature, hearing loss and mental retardation: a new syndrome with autosomal recessive inheritance? *Journal of Oral Pathology & Medicine*. 34(7):444–446. doi:10.1111/j.1600-0714.2005.00318. x.

9. Chan, H.C., Estrella, N.M.R.P., Milkovich, R.N., Kim, J.W., Simmer, J.P., Hu, J.C.C. 2011. Target gene analyses of 39 amelogenesis imperfecta kindreds. *European Journal of Oral Sciences*. 119(Suppl.1):311–323. doi:10.1111/j.1600-0722.2011.00857. x.

10. Chetty, M., Roberts, T.S., Stephen, L.X., Beighton, P.2017. Craniofacial manifestations in osteogenesis imperfecta type III in South Africa. *BDJ Open*. 17021 (2017). doi:10.1038/bdjopen.2017.21

11. Delsuc, F., Gasse, B. & Sire, J.Y. 2015. Evolutionary analysis of selective constraints identifies ameloblastin (*AMBN*) as a potential candidate for amelogenesis imperfecta. *BMC Evolutionary Biology*. 15:148. doi:10.1186/s12862-015-0431-0.

12. Doshi, D.C., Limdi, P.K., Parekh, N. V, Gohil, N.R. 2016. Oculodentodigital dysplasia. *Indian Journal of Ophthalmology*. 64(3):227–230. doi:10.4103/0301-4738.180191.

13. Ferrini, F.R.D., Marba, S.T.M., Gavião, M.B.D. 2008. Oral conditions in very low and extremely low birth weight children. *Journal of Dentistry for Children*. 75(3):235–242.

14. Foster, S.C. 1971. Prader-Willi syndrome: report of cases. *Journal of the American Dental Association*. 83(3):634–638.

15. Gomes-Silva, J.M., Ruviere, D.B., Segatto, A.S., de Queiroz, A.M. de Freitas, A.C. 2006. Sotos syndrome: a case report. *Special Care in Dentistry*. 26(6):257–262.

16. Hirai, N., Matsune, K. & Ohashi, H. 2011. Craniofacial and oral features of Sotos syndrome: differences in patients with submicroscopic deletion and mutation of NSD1 gene. *American Journal of Medical Genetics.Part A*. 155(12):2933–2939. doi:10.1002/ajmg.a.33969.

17. Inokuchi, M., Nomura, J., Mtsumura, Y., Sekida, M., Tagawa, T. 2001. Sotos syndrome with enamel hypoplasia: a case report. *Journal of Clinical Pediatric Dentistry*. 25(4):313–316.

18. Ioannou, S., Sassani, S., Henneberg, M., Henneberg, R.J. 2016. Diagnosing congenital syphilis using Hutchinson's method: differentiating between syphilitic, mercurial, and syphilitic-mercurial dental defects. *American Journal of Physical Anthropology*. 159(4):617–629. doi:10.1002/ajpa.22924.

19. Karnosh, J. 1926. Histopathology of syphilitic hypoplasia of the teeth. *Archives of Dermatology and Syphilology*. 13(1):25–42.

20. Matsune, K., Shimizu, T., Tohma, T., Asada, Y., Ohashi, H., Maeda, T. 2001. Craniofacial and dental characteristics of Kabuki syndrome. *American Journal of Medical Genetics*. 98(2):185–190.

21. Regen, A., Nelson, L.P. & Woo, S.B. 2010. Dental manifestations associated with Seckel syndrome type II: a case report. *Pediatric Dentistry*. 32(5):445–450.

22. Scardina, G., Fuca, G. & Messina, P. 2007. Oral diseases in a patient affected with Prader-Willi syndrome. *European Journal of Paediatric Dentistry.8*(2):96–99.

23. Seymen, F., Tuna, B. & Kayserili, H. 2002. Seckel syndrome: report of a case. *Journal of Clinical Pediatric Dentistry*. 26(3):305–309.

24. Sobral, S.D.P., Leite, A.F., Figueiredo, P.T.S., Ferrari, I., Safatle, H.P.N., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013. Craniofacial and dental features in Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.

25. Spano, G., Campus, G., Bortone, A., Lai, V., Lugliè, P.F. 2008. oral features in Kabuki make-up syndrome. *European Journal of Paediatric Dentistry.* 9(3):149–152.

26. Teixeira, C.S., Silva, C.R., Honjo, R.S., Bertola, D.R., Albano, L.M., Kim, C.A. 2009. Dental evaluation of Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal.* 46(6):668–673. doi:10.1597/08-077.1

27. Torres, C.P., Valadares, G., Martins, M.I., Borsatto, M.C., Díaz-Serrano, K.V., de Queiroz, A.M. 2015. Oral findings and dental treatment in a child with Williams-Beuren syndrome. *Brazilian Dental Journal*. 26(3):312–316. doi:10.1590/0103-6440201300335.

28. Valadares, E.R., Carneiro, T.B., Santos, P.M., Oliveira, A.C., Zabel, B. 2014. What is new in genetics and osteogenesis imperfecta classification? *Jornal de Pediatria*. 90(6):536–541. doi: 10.1016/j.jped.2014.05.003.

29. Vorster, A., Beighton, P., Chetty, M., Ganie, Y., Henderson, B., Honey, E., Maré, P., Thompson, D., et al., 2017. Osteogenesis imperfecta type 3 in South Africa: Causative mutations in *FKBP10. South African Medical Journal*. 107(5), 457-462. doi:10.7196/SAMJ. 2017.v107i5.9461

30. Witkop, C.J. 1988. Amelogenesis imperfecta, dentinogenesis imperfecta and dentin dysplasia revisited: problems in classification. *Journal of Oral Pathology*. 17(9–10):547–553.

31. Wong, D., Ramachandra, S. S., & Singh, A. K. 2015. Dental management of patient with Williams Syndrome - A case report. *Contemporary Clinical Dentistry*, *6*(3), 418–420. http://doi.org/10.4103/0976-237X.161908

CHAPTER 10: ANOMALIES OF THE JAWS AND MIDFACE

Introduction

Various anomalies of the midface and jaw relevant to the investigation are discussed in this chapter.

Congenital anomalies of the jaws and midface are numerous and variable and may be components of specific genetic syndromes. The bones of the jaw and related structures start developing within the first weeks following conception and environmental or genetic interferences during this period may result in morphological changes in this area. The author has included mandibular prognathism, maxillary hypoplasia and cleft palate in a broader category of anomalies of the jaw and midface.

In the survey, 43% (n=69) of the children at the SE Facilities had jaw and midface anomalies. There was a statistically significant difference in proportion participants with anomalies of the jaw and midface across these age categories, p = 0.024. The proportion of participants with anomalies of the jaw and midface in the 3-8 year-age group was statistically significantly lower than the proportion of participants in the 9-11 year-age group, p =0.006. This distribution is explicable as the normal growth spurt for the jaws and midface occurs at this time for children aged between 9 and 13 years (Mellion, Behrents & Johnston, 2013).

There was a weak positive correlation between anomalies of the jaw and midface and malocclusion at the SE Facilities (r_s = 0.29, p < 0.001). This association can be explained by the fact that when either the maxilla or mandible fail to form or grow normally during fetal development, teeth may not erupt in their usual relationships. This may result in malalignment or crowding. Malocclusion will be discussed in chapter 11.

10.1 Mandibular prognathism

Mandibular prognathism is a dentofacial anomaly characterized by protrusion of the mandible, with lower incisors often overlapping the upper incisors. The protruding lower jaw is caused by a forward positioning of the mandible itself (Stiles & Luke, 1953) (Fig 10.1).

Fig 10.1 Mandibular prognathism in a patient at RXH

Mandibular prognathism may be the consequence of malocclusion, genetic mutations and growth disorders such as acromegaly (Smith & Waite, 2012; Agrawal et al., 2013; McKenna, Hayes & Burke, 2014). It may also be a normal phenotypic variant in specific ethnic groups (Chang, Tseng & Chang, 2006). From a familial perspective, mandibular prognathism may occur as an autosomal dominant trait with incomplete expression or non-penetrance (Cruz et al., 2008).

Imbalances in the occlusion of the teeth can force the mandible and its condyles into an anterior, forward location mimicking prognathism. In addition, underdevelopment of the maxilla could contribute to this facial appearance. In these instances, the disorder is known as pseudoprognathism. Both conditions produce a concave appearance of the face (Cruz et al., 2008).

Mutations in several genes have been implicated in the aetiology of mandibular prognathism (Chen et al., 2015; Guan et al., 2015; Perillo et al., 2015). The genetic ID syndromes associated with mandibular prognathism encountered during the investigation are tabulated in Table X.1.

Table X.1: Genetic ID syndromes associated with mandibular prognathism in the survey

Syndrome	Reference
Angelman	Jay et al., 1991; Buntinx et al., 1995; Murakami et al., 2008; de Queiroz et al., 2013
Coffin-Lowry	Hanauer & Young, 2002
Kabuki	do Prado Sobral et al., 2013
Sotos	Villaverde & Da Silva, 1971; Inokuchi et al., 2001; Gomes-silva et al., 2006

10.1.1Dental implications of mandibular prognathism and pseudoprognathism

Mandibular prognathism can have both aesthetic and functional consequences. Apart from an abnormally long chin, the abnormal relationship of the maxillary and mandibular alveolar ridges can result in difficulty in mastication, deglutition and speech. Thus, abnormal occlusion can cause excessive wear on enamel surfaces, increasing the risk of tooth decay. The condition can also cause strain on the temporomandibular joint resulting in additional problems such as the myofascial pain disorder (Tecco et al., 2011).

10.2 Midfacial hypoplasia

Midfacial hypoplasia is a designation denoting underdevelopment of the maxillary bones. It results in retrusion of the central aspect of the face and can create a false impression of mandibular prognathism.

The bones affected by the deficient growth are the nasal bones, maxillary bones and the zygomata. The underdeveloped bones push the tongue into a posterior position, resulting in breathing difficulty and airway obstruction. The syndromic diagnoses in children with midfacial hypoplasia encountered in this study are listed in Table X.2

Table X.2: Genetic ID syndromes associated with midface hypoplasia encountered during the survey

Syndrome	Reference
Apert	Martelli et al., 2008; Dixit et al., 2008; Soancă et al., 2010; Khan et al., 2012; Carpentier et al., 2014
Coffin-Lowry	Hanauer & Young, 2002
Down	Suri,Tompson, & Cornfoot, 2010; Alió et al., 2011; Unkel et al., 2012
Kabuki	Matsune et al., 2001; Petzold et al., 2003; Atar, Lee & O'Donnell, 2006; Tuna et al., 2012; do Prado Sobral et al., 2013; Sattur et al., 2014
Rubinstein-Taybi	O'Neil et al., 1989; Allanson & Hennekam, 1997; Zwierzchowski et al., 2015
Simpson-Golabi-Behmel	Krimmel & Reinert, 2000; Bayram, Yildirim & Seymen, 2015

10.2.1 Dental implications of midface hypoplasia

Apart from aesthetic and dental problems, children with midface hypoplasia may often experience difficulties in breathing and airway obstruction. These factors can pose problems during general anaesthesia procedures (chapters 13 and 14).

10.3 Management implications of mandibular prognathism and midfacial hypoplasia in ID

The management of both mandibular prognathism and maxillary hypoplasia necessitates a multidisciplinary team comprising orthodontists, prosthodontists and maxillofacial surgeons. Operative procedures are complex and warrant prior consideration when planning treatment for children with ID. Reconstruction of the face is performed under general anaesthesia. During this procedure, airway obstruction may develop and intubation may be difficult. Other problems which may occur during these procedures are discussed in chapter 13.

10.4 Cleft palate and lip

Clefting of the palate and lip (Fig 10.2A and 10.2B) are congenital developmental anomalies resulting from incomplete fusion of the structures which form the upper lip and palate during embryogenesis. This process occurs at approximately 35 days of gestation for the lip and in the palate by the eighth or ninth week of pregnancy. Clefts of the palate can involve either the hard or soft palate or both and can be located in various positions in these structures. All the participants in this study who presented with clefts had been managed surgically during early childhood.

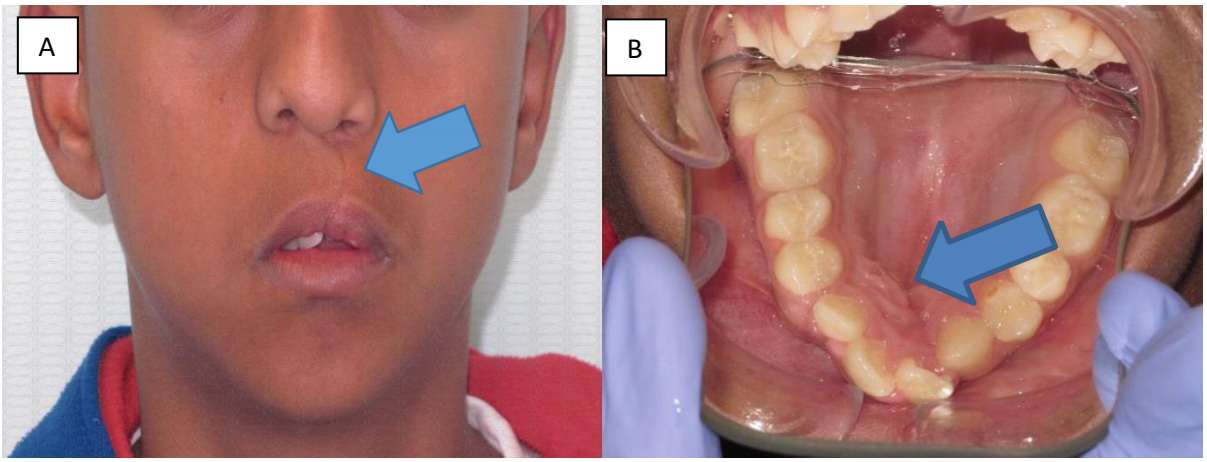


Fig 10.2 Repair of a unilateral cleft lip (A) and palate (B).

Courtesy: Dr T di Pasquale

Palatal clefts are either complete (involving the entire palate) or incomplete (involving either the soft or hard palate) and result from the incomplete fusion of the lateral palatine processes, the septal bone of the nose and the median palatine processes. These abnormalities can be either be unilateral or bilateral. In either instance, they result in velopharyngeal communication between the mouth and the nasal cavity. When clefts occur, they are frequently accompanied by a split uvula. Submucous cleft palate (SMCP), an incomplete cleft of the soft palate, presents as a groove along the midline of the soft palate. The condition is typically accompanied by a bifid uvula and a notch in the posterior margin of the hard palate. Genetic ID syndromes accompanied by cleft lip and or cleft palate observed in this study are listed in Table X.3.

Table X.3: Genetic ID syndromes associated with cleft lip and or palate

Syndrome	Reference
Apert	Letra et al., 2007; Carpentier et al., 2014; Tsukamoto & Yokoyama, 2015
Kabuki	Iida et al., 2006; Atar, Lee & O'Donnell, 2006; Spano et al., 2008; Teixeira et al., 2009; Abdel-Salam et al., 2011; do Prado Sobral et al., 2013
Rubinstein Taybi	De Coster et al., 2009
Seckel	Garg et al., 2012; Grewal et al., 2014
Simpson-Golabi-Behmel	Morita et al., 2011
Williams	Vincent, Mercier & David, 2008; Domenico et al., 2013
Wolf-Hirschhorn	Johnston & Franklin, 2006; Paradowska-Stolarz, 2014

10.4.1 Dental implications of cleft lip and cleft palate

The field of cleft lip and palate is both vast and complex. In this context of this investigation, these malformations were included in the broader category of dentoalveolar and oral anomalies. Aesthetics, psychological problems, feeding and breathing difficulties are the most common complications of cleft lip and palate. In addition, there is an increased frequency of dental anomalies in children with cleft palates (Jabbari et al., 2016)

In general, clefts may result in deviations in the quantity, morphology, dimension and location of teeth in the affected area (Fig 10.3).

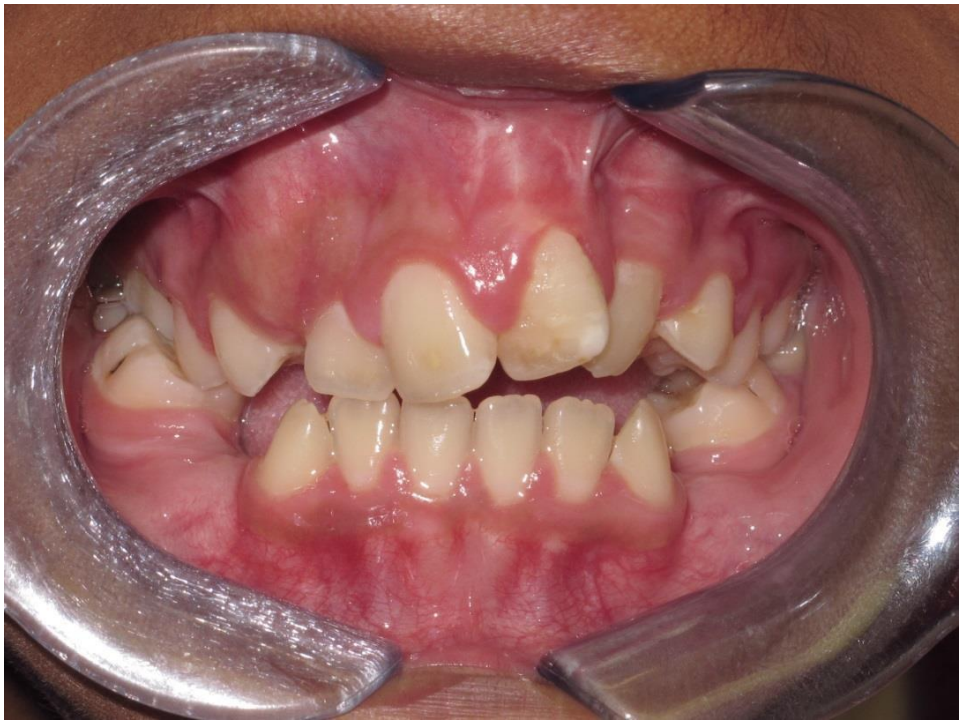


Fig 10.3 Malocclusion resulting from a unilateral cleft lip and palate.
Courtesy Dr T di Pasquale

The most common dental anomaly accompanying cleft palate is hypodontia (chapter 7) which occurs in approximately 80% of children affected by non-syndromic palatal clefts (Shapira, Lubit & Kuftinec, 1999). Although not specifically documented, the results of this investigation may suppport these findings (correlation between missing teeth and anomalies of the jaw and midface rs=0.17, p=0.0300). Paradoxically, supernumerary teeth are also common in this condition (Kirchberg, Treide & Hemprich, 2004; Tannure et al., 2012) and clefts may also be associated with specific skeletal features (Al-Ani et al., 2017). Dental caries and gingival disease are more prevalent in children with palatal clefts (Hasslöf & Twetman, 2007).

10.4.2 Management implications of cleft lip and cleft palate in ID

The management of cleft lips and cleft palates involves a team of specialist surgeons, nurses, speech therapists, genetic counsellors and parents. Oral health care professionals play a

pivotal role in maintaining optimal oral hygiene in the affected children from an early age. This is important in order to prevent the unnecessary loss of teeth and bone. In turn, this approach will stabilize the size of the cleft and reduce the amount of bone required for grafting when surgery in undertaken (Jabbari et al., 2016). As the child ages, more sophisticated dental procedures may be necessary, depending on the dental anomalies accompanying the repaired cleft.

The management of the cleft palate may be difficult, especially in ID. Numerous ID syndromes are associated with anaesthetic risks such as breathing problems and airway obstruction. Additional dental management challenges in children with repaired cleft palates pertained to the correction of anomalies such as hypodontia and supernumerary teeth. These procedures may require protracted periods of rehabilitation and or repeated general anaesthesia.

Concluding comments:

This chapter highlighted the dental implications of 3 types of skeletal variations that were encountered during the investigation together with their dental and management implications.

References

1. Abdel-Salam, G.M., Afifi, H.H., Eid, M.M., El-Badry, T.H., Kholoussi, N. 2011. Ectodermal abnormalities in patients with Kabuki syndrome. *Pediatric Dermatology*. 28(5):507–511. doi: 10.1111/j.1525-1470.2011.01495. x.
2. Agrawal, M., Maitin, N., Rastogi, K., Bhushan, R. 2013. Seeing the unseen: diagnosing acromegaly in a dental setup. *BMJ Case Reports*. 2013. doi: 10.1136/bcr-2013-200266.
3. Alió, J., Lorenzo, J., Iglesias, M.C., Manso, F.J., Ramírez, E.M. 2011. Longitudinal maxillary growth in Down syndrome patients. *Angle Orthodontist*. 81(2):253–259. doi: 10.2319/040510-189.1.
4. Allanson, J.E. & Hennekam, R.C. 1997. Rubinstein-Taybi syndrome: objective evaluation of craniofacial structure. *American Journal of Medical Genetics*. 71(4):414–419.
5. Atar, M., Lee, W. & O'Donnell, D. 2006. Kabuki syndrome: Oral and general features seen in a 2-year-old Chinese boy. *International Journal of Paediatric Dentistry*. 16(3):222–226. doi: 10.1111/j.1365-263X.2006.00699. x.
6. Bayram, M., Yildirim, M. & Seymen, F. 2015. Clinical and oral findings of a patient with Simpson-Golabi-Behmel syndrome. *European Archives of Paediatric Dentistry.* 16(1):63–66. doi: 10.1007/s40368-014-0141-0.
7. Buntinx, I.M., Hennekam, R.C., Brouwer, O.F., Stroink, H., Beuten, J., Mangelschots, K., Fryns, J.P. 1995. Clinical profile of Angelman syndrome at different ages. *American Journal of Medical Genetics*. 56(2):176–183. doi: 10.1002/ajmg.1320560213.
8. Carpentier, S., Schoenaers, J., Carels, C., Verdonck, A. 2014. Cranio-maxillofacial, orthodontic and dental treatment in three patients with Apert syndrome. *European Archives of Paediatric Dentistry.* 15(4):281–289. doi: 10.1007/s40368-013-0105-9.
9. Chang, H.P., Tseng, Y.C. & Chang, H.F. 2006. Treatment of mandibular prognathism. *Journal of the Formosan Medical Association*. 105(10):781–790. doi: 10.1016/S0929-6646(09)60264-3.
10. Chen, F., Li, Q., Gu, M., Li, X., Yu, J., Zhang, Y.B. 2015. Identification of a mutation in *FGF23* involved in mandibular prognathism. *Scientific Reports*. 5:11250. doi: 10.1038/srep11250.
11. Cruz, R.M., Krieger, H., Ferreira, R., Mah, J., Hartsfield, J., Oliveira, S. 2008. Major gene and multifactorial inheritance of mandibular prognathism. *American Journal of Medical Genetics. Part A*. 146(1):71–77. doi: 10.1002/ajmg.a.32062.
12. De Coster, P.J., Marks, L.A., Martens, L.C., Huysseune, A. 2009. Dental agenesis: genetic and clinical perspectives. *Journal of Oral Pathology and Medicine*. 38(1):1–17. doi: 10.1111/j.1600-0714.2008.00699. x.
13. de Queiroz, A.M., de Siqueira Melara, T., Fernandes Ferreira, P.D., Lucisano, M.P., De Rossi, A., Nelson-Filho, P., Bezerra Silva, R.A. 2013. Dental findings and special care in patients with Angelman syndrome: a report of three cases. *Special Care in Dentistry.* 33(1):40–45. doi: 10.1111/j.1754-4505.2012.00292. x.

14. Dixit, S., Singh, A., Mamatha, G.S., Desai, R., Jaju, P. 2008. Apert syndrome: report of a new case and its management. *International Journal of Clinical Pediatric Dentistry*. 1(1):48–53. doi: 10.5005/jp-journals-10005-1009.
15. Domenico, S., Orlando, C., Graziana, F.F.M., Papi, P., Giulia, A. 2013. Cleft palate in Williams syndrome. *Annals of Maxillofacial Surgery*. 3(1):84–8 6. doi: 10.4103/2231-0746.110071.
16. do Prado Sobral, S., Leite, A.F., Figueiredo, P.T., Ferrari, I., Safatle, H.P., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al., 2013. Craniofacial and dental features in Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal.* 50(4):440–447. doi: 10.1597/11-052.
17. Garg, R., Uppal, S., Mittal, R., Grewal, A., Sood, D., Shah, S. 2012. Palatoplasty in a patient with Seckel syndrome. *Annals of Maxillofacial Surgery*. 2(1):63–65. doi: 10.4103/2231-0746.95324.
18. Gomes-Silva, J.M., Ruviere, D.B., Segatto, R.A., de Queiroz, A.M., de Freitas, A.C. 2006. Sotos syndrome: a case report. *Special Care in Dentistry*. 26(6):257–262.
19. Grewal, A., Sood, D., Bhatia, N., Garg, R., Shah, S., Kaur, H. 2014. Palatoplasty in a patient with Seckel syndrome: an anesthetic challenge. *Brazilian Journal of Anesthesiology*. 64(3):216–218. doi: 10.1016/j.bjane.2013.08.005.
20. Guan, X., Song, Y., Ott, J., Zhang, Y., Li, C., Xin, T., Li, Z., Gan, Y., et al., 2015. The *ADAMTS1* gene is associated with familial mandibular prognathism. *Journal of Dental Research*. 94(9):1196–1201. doi: 10.1177/0022034515589957.
21. Hanauer, A. & Young, I.D. 2002. Coffin-Lowry syndrome: clinical and molecular features. *Journal of Medical Genetics*. 77(10):705–713. doi: 10.1136/jmg.39.10.705.
22. Hasslöf, P. & Twetman, S. 2007. Caries prevalence in children with cleft lip and palate--A systematic review of case-control studies. *International Journal of Paediatric Dentistry.* 17(5):313–319. doi: 10.1111/j.1365-263X.2007.00847.x.
23. Iida, T., Park, S., Kato, K., Kitano, I. 2006. Cleft palate in Kabuki syndrome: a report of six cases. *Cleft Palate-craniofacial Journal.* 43(6):756–761. doi: 10.1597/05-174.
24. Inokuchi, M., Nomura, J., Mtsumura, Y., Sekida, M., Tagawa, T. 2001. Sotos syndrome with enamel hypoplasia: a case report. *Journal of Clinical Pediatric Dentistry*. 25(4):313–316.
25. Jabbari, F., Reiser, E., Thor, A., Hakelius, M., Nowinski, D. 2016. Correlations between initial cleft size and dental anomalies in unilateral cleft lip and palate patients after alveolar bone grafting. *Upsala Journal of Medical Sciences*. 121(1):33–37. doi: 10.3109/03009734.2015.1134733.
26. Jay, V., Becker, L.E., Chan, F.W., Perry, T.L. 1991. Puppet-like syndrome of Angelman: a pathologic and neurochemical study. *Neurology*. 41(3):416–422.
27. Johnston, N.J. & Franklin, D.L. 2006. Dental findings of a child with Wolf-Hirschhorn syndrome. *International Journal of Paediatric Dentistry.* 16(2):139–142. doi: 10.1111/j.1365-263X.2006.00675. x.
28. Khan, S., Chatra, L., Shenai, P., Veena, K. 2012. Apert syndrome: a case Report. *International Journal of Clinical Pediatric Dentistry*. 5(3):203–206. doi: 10.5005/jp-journals-10005-1166.

29. Kirchberg, A., Treide, A. & Hemprich, A. 2004. Investigation of caries prevalence in children with cleft lip, alveolus, and palate. *Journal of Cranio-maxillo-facial Surgery.* 32(4):216–219. doi: 10.1016/j.jcms.2004.02.003.
30. Krimmel, M. & Reinert, S. 2000. Multiple odontogenic keratocysts In Mental Retardation-Overgrowth (Simpson-Golabi-Behmel) syndrome. *British Journal of Oral & Maxillofacial Surgery*. 38(3):221–223. doi: 10.1054/bjom.1999.0186.
31. Letra, A., de Almeida, A.L., Kaizer, R., Esper, L.A., Sgarbosa, S., Granjeiro, J.M. 2007. Intraoral features of Apert's syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 103(5):e38-41. doi: S1079-2104(06)00287-3.
32. Martelli, H., Paranaíba, L.M.R., de Miranda, R.T., Orsi, J, Coletta, R.D. 2008. Apert syndrome: report of a case with emphasis on craniofacial and genetic features. *Pediatric Dentistry*. 30(6):464–468.
33. Matsune, K., Shimizu, T., Tohma, T., Asada, Y., Ohashi, H., Maeda, T. 2001. Craniofacial and dental characteristics of Kabuki syndrome. *American Journal of Medical Genetics*. 98(2):185–190.
34. McKenna, G., Hayes, M. & Burke, F.M. 2014. Prosthodontic rehabilitation for a patient with acromegaly. *European Journal of Prosthodontics and Restorative Dentistry*. 22(3):98–100.
35. Mellion, Z.J., Behrents, R.G. & Johnston, L.E. 2013. The pattern of facial skeletal growth and its relationship to various common indexes of maturation. *American Journal Orthodontics and Dentofacial Orthopedics.* 143(6):845-854. doi: 10.1016/j.ajodo.2013.01.019.
36. Morita, Y., Kimoto, N., Ogawa, H., Omata, T., Morita, N. 2011. Simpson-Golabi-Behmel syndrome associated with cleft Palate. *Journal of Craniofacial Surgery*. 22(5):1917–1918. doi: 10.1097/SCS.0b013e31822ea73c.
37. Murakami, C., Nahás Pires Corrêa, M.S., Nahás Pires Corrêa, F., Nahás Pires Corrêa, J.P. 2008. Dental treatment of children with Angelman syndrome: a case report. *Special Care in Dentistry*. 28(1):8–11. doi: 10.1111/j.1754-4505.2008.00003. x.
38. O'Neil, D.W., Canada, R.T., Clark, M. V., Lowe, J.W. 1989. Rubinstein-Taybi syndrome: case report. *Pediatric Dentistry*. 11(2):158–160.
39. Paradowska-Stolarz, A.M. 2014. Wolf-Hirschhorn syndrome (WHS) - literature review on the features of the syndrome. *Advances in Clinical and Experimental Medicine*. 23(3):485–489.
40. Perillo, L., Monsurrò, A., Bonci, E., Torella, A., Mutarelli, M., Nigro, V. 2015. Genetic association of *ARHGAP21* gene variant with mandibular prognathism. *Journal of Dental Research*. 94(4):569–576. doi: 10.1177/0022034515572190.
41. Petzold, D., Kratzsch, E., Opitz, C., Tinschert, S. 2003. The Kabuki syndrome: four patients with oral abnormalities. *European Journal of Orthodontics*. 25(1):13–19.
42. Sattur, A., Deshmukh, P.K., Abrahim, L.,Naikmasur, V.G. 2014. Kabuki make-up syndrome - a case report with electromyographic study. *Journal of Clinical and Diagnostic Research*. 8(11):ZD03-ZD06. doi: 10.7860/JCDR/2014/9804.512.

43. Smith, C.B. & Waite, P.D. 2012. Surgical management of obstructive sleep apnea in acromegaly with mandibular prognathism and macroglossia: a treatment dilemma. *Journal of Oral and Maxillofacial Surgery.* 70(1):207–210. doi: 10.1016/j.joms.2011.05.022.
44. Shapira, Y., Lubit, E. & Kuftinec, M.M.1999. Congenitally missing second premolars in cleft lip and cleft palate children. *American Journal of Orthodontics and Dentofacial Orthopedics.* 115(4):396-400.
45. Soancă, A., Dudea, D., Gocan, H., Roman, A., Culic, B. 2010. Oral manifestations in Apert syndrome: case presentation and a brief review of the literature. *Romanian Journal of Morphology and Embryology.* 51(3):581–584. doi: 510310581584.
46. Spano, G., Campus, G., Bortone, A., Lai, V., Lugliè, P.F. 2008. Oral features in Kabuki make-up syndrome. *European Journal of Paediatric Dentistry.* 9(3):149–152.
47. Stiles,K. A. & Luke,J.E. 1953. The inheritance of malocclusion due to mandibular prognathism. *Journal of Hereditary.* 44:241–245.
48. Suri, S., Tompson, B.D. & Cornfoot, L. 2010. Cranial base, maxillary and mandibular morphology in Down syndrome. *Angle Orthodontist*. 80(5):861–869. doi: 10.2319/111709-650.1.
49. Tannure, P.N., Oliveira, C.A.G.R., Maia, L.C., Vieira, A.R., Granjeiro, J.M., Costa, M. 2012. Prevalence of dental anomalies in nonsyndromic individuals with cleft lip and palate: a systematic review and meta-analysis. *Cleft Palate-Craniofacial Journal.* 49(2):194–200. doi: 10.1597/10-043.
50. Tecco, S., Crincoli, V., Di Bisceglie, B., Saccucci, M., MacrÍ, M., Polimeni, A., Festa, F. 2011. Signs and symptoms of temporomandibular joint disorders in caucasian children and adolescents. *Cranio.* 29(1):71–79. doi: 10.1179/crn.2011.010.
51. Teixeira, C.S., Silva, C.R., Honjo, R.S., Bertola, D.R., Albano, L.M., Kim, C.A. 2009. Dental evaluation of Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal.* 46(6):668–673. doi: 10.1597/08-077.1.
52. Tsukamoto, M. & Yokoyama, T. 2015. Alternative methods for nasotracheal intubation and extubation in a patient with Apert syndrome. *Anesthesia Progress.* 62:122–124. doi: 10.2344/0003-3006-62.3.122.
53. Tuna, E.B., Marşan, G., Gençay, K., Seymen, F. 2012. Craniofacial and dental characteristics of Kabuki syndrome: nine years cephalometric follow-up. *Journal of Clinical Pediatric Dentistry*. 36(4):393–400.
54. Unkel, J.H., Edwards, J.S., Piscitelli, W.P., Tye, G.W. 2012. Dental surgery and anesthetic precautions of a patient with Down syndrome and juvenile rheumatoid arthritis: a case report. *Pediatric Dentistry*. 34(7):517–520.
55. Villaverde, M.M. & Da Silva, J.A. 1971. Sotos syndrome: hypertelorism, antimongoloid slant of eye, and high arched palate complex. *Journal of the Medical Society of New Jersey*. 68(10):805–808.
56. Vincent, C., Mercier, J.M. & David, A. 2008. Cleft palate and Williams syndrome. [Abstract]. *Revue De Stomatologie et de Chirurgie Maxillo-faciale*. 109(1):44–47. doi: 10.1016/j.stomax.2007.10.005.
57. Zwierzchowski, T.J., Przedborska, A., Wilmańska, I., Raczkowski, J.W. 2015. Rubinstein-Taybi syndrome in a 19-year old boy. *Neuro Endocrinology Letters*. 36(5):417–420.

CHAPTER 11: MALOCCLUSION, ANOMALIES OF SALIVA AND MACROGLOSSIA

11.1 Malocclusion

A plethora of factors may give rise to malocclusion (Fig 11.1) including a disproportionate relationship between the size of teeth and the length of the alveolar arches and changes in the soft tissues of the face and mouth. Localized causes of malocclusion include anomalies of number, shape and size of teeth and premature loss of primary teeth. There is a distinct difference between dental and skeletal malocclusion. Dental malocclusion occurs when there is improper positioning of the teeth in the jaw. Skeletal malocclusion is caused by alterations in position of the mandible and/or maxilla during embryonic development resulting in a disproportionate growth of the facial bones (Mageet, 2016). In the context of the current investigation, malocclusion referred to disharmony of occlusion irrespective of the aetiology.

Although malocclusion is present in the general population, there appears to be a higher prevalence in people with ID (Winter, Baccaglini & Tomar, 2008; Vellappally et al., 2014).

Approximately 30% of participants at the SE Facilities and 76 % of children at the RXH presented with malocclusion. The prevalence of malocclusion at both investigation sites was lower than that in children with ID from other geographic areas (Desai, Messer & Calache, 2001; Oredugba & Akindayomi, 2008; Purohit, Acharya & Bhat, 2010).

In the project malocclusion at RXH was statistically significantly higher compared to the other 6 sites, $p < 0.0001$. In addition, there was a positive correlation between anomalies of the jaw and midface (r_s=0.29; p<0.001) at the SE Facilities. These findings may indicate that the aetiology of malocclusion in this investigation may have been the result of skeletal abnormalities.

At both sites, the frequency of malocclusion increased as the children grew older and there was a correlation between malocclusion and age at the SE Facilites (r_s=0.1943; p=0.0154). These findings occur with those of Ghiz et al., 2005 who noted that the relationship between the mandible and the maxilla in younger children is not significantly different, but become more evident after the age of 12 years. The prevalence of malocclusion was similar among both males and females at both investigation sites.

The correlation between malocclusion and gingival disease at the SE Facilities (r_s=0.2209; p=0.006) was discussed in chapter 6.

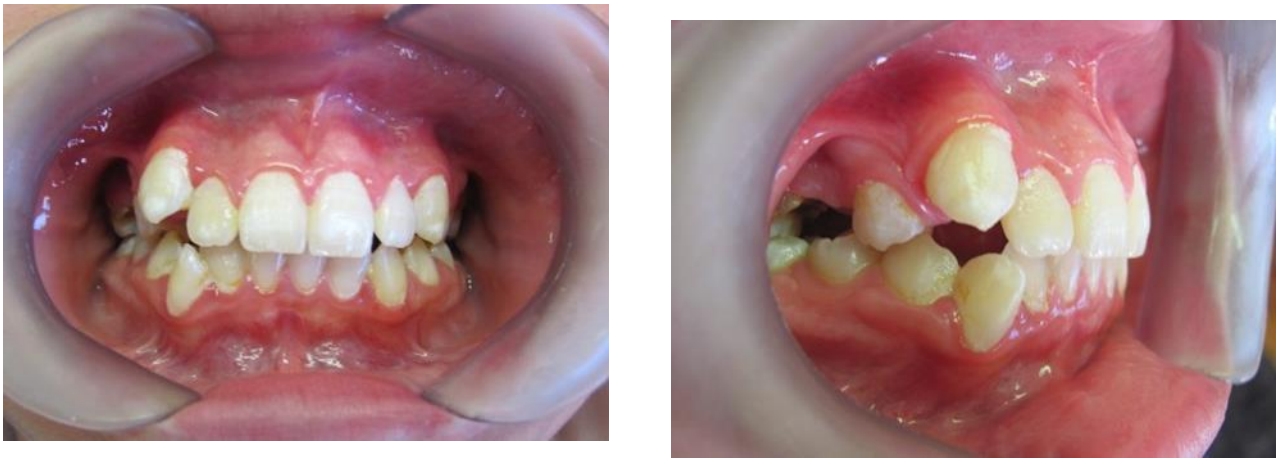


Fig 11.1: A girl aged 14 years with the Williams syndrome and malocclusion at RXH

11.1.1 Dental implications of malocclusion in ID

The problems associated with malocclusion depend upon its type and severity. Crowding of teeth can increase the difficulty of brushing and flossing. Excessive spaces between the teeth can serve as sites for impaction of food. Together these may potentiate the development and progression of dental caries and gingival disease. Other dental consequences include

temporomandibular disorders (Simmons et al., 2008) and bruxism (Ghafournia & Hajenourozali Tehrani, 2012).

The potential systemic consequences of malocclusion may affect the general well-being of children with ID and have an impact on their management under general anaesthesia.

The effects of malocclusion on the digestive system were described by (Koike et al., 2013) who detected a marked association between malocclusion and gastric emptying function. The author speculated that malaligned teeth may cause the inadequate mastication of food and result in an increase of the functional burden on the stomach and lead to digestive problems.

There is a higher frequency of sleep-related breathing disorders in children with occlusal disharmonies (Sauer et al., 2012) that may result in airway obstruction and sleep apnea (Joshi et al., 2014). In turn sleep apnea is an important consideration when managing children with ID under general anaesthesia. Furthermore, narrowing of the upper respiratory tract has been reported is specific categories of skeletal malocclusion (Guyer et al., 1986; de Freitas et al., 2006; Simmons, Oxford & Hill, 2008) and may complicate intubation.

11.1.2 Management implications of malocclusion in children with ID

The management of malocclusion in children with ID is determined by the nature and severity of the disability. Orthodontic treatment to correct malocclusion in children with ID is comparable to non-ID children, and any limitation should not be considered as an impediment to receiving optimal care (Kleint, Kanitz & Harzer, 2002). In addition, surgical correction of other skeletal abnormalities may either precede or follow orthodontic intervention. Irrespective of the management protocol, meticulous tooth brushing and flossing should be sustained. In these situations, caregivers may need to participate in maintaining acceptable

levels of oral hygiene in the affected children. Despite these considerations, none of the participants in the project received these forms of management. Moreover, there was no access to dedicated treatment, primarily due to the expense involved in private treatment and long waiting periods at tertiary hospitals.

11.2 Changes in salivary flow

Effective speech, mastication, and swallowing requires salivary lubrication. These factors also protect the oral soft tissues from dehydration and injury. Xerostomia and sialorrhoea are two key complications of changes in salivary flow that affect the oral health of children with ID.

11.2.1 Xerostomia

In the author's investigation xerostomia, or dry mouth was frequent in participants with the Prader-Willi syndrome. This feature has also been documented in other studies among persons with this disorder (Young et al. 2001; Scardina et al. 2007; Olczak-Kowalczyk et al. 2011 and Saeves et al. 2012). In all these investigations dental caries was a frequent complication of xerostomia. Additional complications of dry mouth include poor oral hygiene, oral candidiasis, atrophy of lingual filiform papillae, angular stomatitis and halitosis. Xerostomia results in the formation of thick, viscous saliva that stimulates the proliferation of oral microorganisms and in rare instances, an ascending (suppurative) sialadenitis may ensue. Xerostomia is managed conservatively either by stimulating salivary flow or the use of artificial saliva.

11.2.2 Sialorrhea

Hypersalivation (Fig 11.2) is caused by either the excessive production of saliva, the failure to keep saliva in the oral cavity, ineffective swallowing infections or allergic reactions. In the

author's investigation, hypersalivation was commonly seen in children with the Down syndrome. These children often had delayed swallowing reflexes and incompetent lips whie ineffective control of the jaws further complicated these problems. Hypersalivation can also result in softening or cracking of the lips.

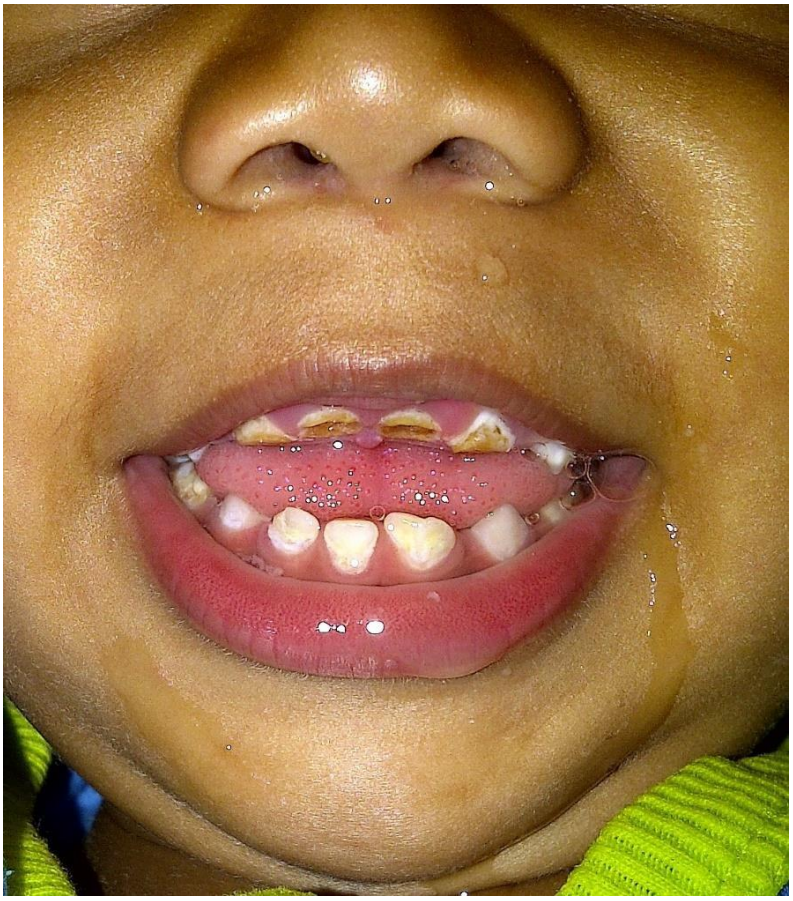


Fig 11.2 A boy aged 4 years with hypersalivation

Psychosomatic problems associated with sialorrhea include social seclusion and a high level of dependency on caregivers. These factors could result in lowered self-esteem and difficulties relationships.

In comparison to its harmful effects, sialorrhea may be accompanied by higher quantities of salivary IgA that protect teeth from dental caries (Cogulu et al., 2006). Similarly, the higher

levels of bicarbonate ions in the excess saliva can increase the pH of the oral environment, further averting tooth demineralization.

Several methods for managing excessive salivation are available. Assessment of an appropriate volume of salivary flow for mastication, swallowing and oral hygiene is essential, irrespective of the management of choice.

Dental implications of Sialorrhea

People with drooling problems are more likely to aspirate saliva, food, or fluids, especially when the body's natural reflex mechanisms, such as gagging and coughing, are also impaired. This condition may compromise the dental management of the affected children in both the consultation rooms and during general anaesthesia (chapter 13). Certain dental materials used to treat carious lesions are sensitive to moisture, and if saliva is not adequately controlled, this could compromise the stability of these compounds.

11.3 Macroglossia

Macroglossia (Fig 11.3) or an unusually large tongue can cause aesthetic and functional problems. Pseudomacroglossia is a term used when the size of the tongue is normal but large in relation to diminished dimensions of the other oral structures.

True macroglossia can accompany an underlying systemic disorder such as amyloidosis but it may also be a component of a genetic syndrome. Functional macroglossia follows a surgical reduction to the oral cavity resulting in decreased space for the tongue adaptation of the tongue (Medeiros et al., 2000).

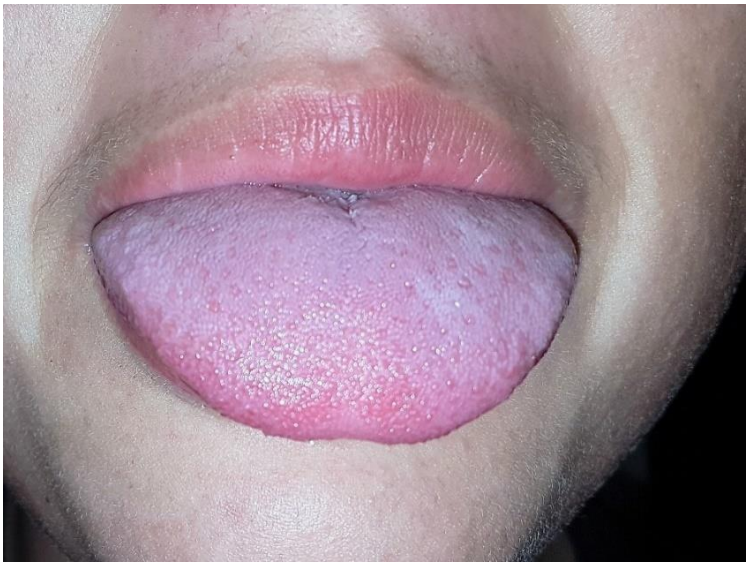


Fig 11.3 A boy aged 14 years with macroglossia

Genetic ID syndromes associated with macroglossia encountered in this study are listed in Table X.1.

Table XI.1: Examples of genetic ID syndromes associated with macroglossia

Syndrome	**Reference**
Angelman	Buntinx et al. 1995; Ohshita et al. 2010
Costello	Hennekam 2003;Della Marca et al. 2006; Takahashi and Ohashi 2013; Williams, 2014
Down	Mixter, Ewanowski & Carson, 1993; Moura et al. 2008; Guimaraes et al., 2008; Starbuck,Reeves & Richtsmeier, 2011
Hunter	Yoskovitch et al. 1998; Wold et al. 2010; Gajula et al. 2012; Ribeiro et al. 2014; Savitha et al. 2015
Hurler	Nargozian 2004; Guven et al. 2008; Wadenya et al. 2010; Wold et al. 2010; Ribeiro et al. 2014; Thakur et al. 2015
Kabuki	Kobayashi et al. 2001; Abdel-Salam et al. 2011
Simpson-Golabi-Behmel	Butler et al. 2000; Paludetti et al. 2003; Yano et al. 2011; Knopp et al. 2015; Bayram et al. 2015
Williams	Vieira et al. 2015

11.3.1 Dental implications of macroglossia in ID

In the dental context, macroglossia may result in excessive dyspnea, drooling and gagging. An abnormally large tongue can impede access to the mouth of the affected child for both oral hygiene and dental care. Routine brushing and flossing, especially in the posterior areas of the mouth, may become difficult thereby increasing the risk of dental caries and gingival disease. Macroglossia may also interfere with the use of dental instruments during routine dental management. Excessive pressure exerted by the enlarged tongue may cause teeth to drift apart, resulting in faulty dental occlusion. In turn, malocclusion can result in dysfunction and damage of the temporomandibular joint. Additional problems that may develop include mandibular prognathism, mouth breathing and diastema (Topouzelis, Iliopoulos, & Kolokitha, 2011).

Children with ID often require general anaesthesia for routine dental procedures (chapter 13). In these circumstances an enlarged tongue may occupy the posterior aspect of the oral cavity, causing obstruction of the upper airways (Jacobs, Gray & Todd, 1996; Gadiwalla et al., 2016).

The management of macroglossia depends on its aetiology. When associated with local factors such as obstruction of salivary glands, the underlying causes are addressed. Excessively distended tongues that are components of systemic disorders usually require surgical reduction.

References:

1. Abdel-Salam, G.M., Afifi, H.H., Eid, M.M., El-Badry, T.H., Kholoussi, N. 2011. Ectodermal abnormalities in patients with Kabuki syndrome. *Pediatric Dermatology*. 28(5):507–511. doi:10.1111/j.1525-1470.2011.01495. x.

2. Bayram, M., Yildirim, M. & Seymen, F. 2015. Clinical and oral findings of a patient with Simpson-Golabi-Behmel syndrome. *European Archives of Paediatric Dentistry.* 16(1):63–66. doi:10.1007/s40368-014-0141-0 [doi].

3. Buntinx, I.M., Hennekam, R.C., Brouwer, O.F., Stroink, H., Beuten, J., Mangelschots, K., Fryns, J.P. 1995. Clinical profile of Angelman syndrome at different ages. *American Journal of Medical Genetics*. 56(2):176–83. doi:10.1002/ajmg.1320560213.

4. Butler, M.G., Hayes, B.G., Hathaway, M.M., Begleiter, M.L. 2000. Specific genetic diseases at risk for sedation/anesthesia complications. *Anesthesia and Analgesia*. 91(4):837–855. doi:10.1097/00000539-200010000-00014.

5. Cogulu, D., Sabah, E., Kutukculer, N., Ozkinay, F. 2006. Evaluation of the relationship between caries indices and salivary secretory IgA, salivary pH, buffering capacity and flow rate in children with Down's syndrome. *Archives of Oral Biology*. 51(1):23–28. doi: 10.1016/j.archoralbio.2005.06.001.

6. de Freitas, M.R., Alcazar, N.M.P.V., Janson, G., de Freitas, K.M.S., Henriques, J.F.C. 2006. Upper and lower pharyngeal airways in subjects with Class I and Class II malocclusions and different growth patterns. *American Journal of Orthodontics and Dentofacial Orthopedics.* 130 (6): 742–745. doi: 10.1016/j.ajodo.2005.01.033

7. Della Marca, G., Rubino, M., Vollono, C., Vasta, I., Scarano, E., Mariotti, P., Cianfoni, A., Mennuni, G.F., et al. 2006. Rhythmic tongue movements during sleep: a peculiar parasomnia in Costello syndrome. *Movement Disorders*. 21(4):473–478. doi:10.1002/mds.20741.

8. Desai, M., Messer, L.B. & Calache, H. 2001. A study of the dental treatment needs of children with disabilities in Melbourne, Australia. Australian Dental Journal. 46(1):41–50. doi:10.1111/j.1834-7819. 2001.tb00273. x.

9. Gadiwalla, Y., Burnham, R., Warfield, A., Praveen, P. 2016. Surgical Management of macroglossia secondary to amyloidosis. *BMJ Case Reports*. 2016. doi:10.1136/bcr-2015-214078.

10. Gajula, P., Ramalingam, K. & Bhadrashetty, D. 2012. A rare case of mucopolysaccharidosis: Hunter syndrome. *Journal of Natural Science, Biology, and Medicine*. 3(1):97–100. doi:10.4103/0976-9668.95984.

11. Ghafournia, M. & Hajenourozali Tehrani, M.2012. Relationship between Bruxism and Malocclusion among Preschool Children in Isfahan. *Journal of Dental Research, Dental Clinics, Dental Prospects*. 6(4): 138–142. doi:10.5681/joddd.2012.028

12. Ghiz, M.A., Ngan, P.& Gunel, E., 2005. Cephalometric variables to predict future success of early orthopedic Class III treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*. 127 (3):301–306. doi: 10.1016/j.ajodo.2004.02.014

13. Guimaraes, C.V.A., Donnelly, L.F., Shott, S.R., Amin, R.S., Kalra, M. 2008. Relative rather than absolute macroglossia in patients with Down syndrome: implications for treatment of obstructive sleep apnea. *Pediatric Radiology*. 38(10):1062–1067. doi:10.1007/s00247-008-0941-7.

14. Guven, G., Cehreli, Z.C., Altun, C., Şençimen, M., Ide, S., Bayari, S.H., Karaçay, Ş,. 2008. Mucopolysaccharidosis type I (Hurler syndrome): oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*. 105(1):72–78. doi: 10.1016/j.tripleo.2007.02.015.

15. Hennekam, R.C.M. 2003. Costello syndrome: an overview. *American Journal of Medical Genetics. Part C.* 117(1):42–48. doi:10.1002/ajmg.c.10019.

16. Jacobs, I.N., Gray, R.F. & Todd, N.W. 1996. Upper airway obstruction in children with Down syndrome. *Archives of Otolaryngology-Head & Neck Surgery*. 122(9):945–950.

17. Joshi, N., Hamdan, A.M. & Fakhouri, W.D. 2014. Skeletal Malocclusion: A Developmental Disorder with a Life-Long Morbidity. *Journal of Clinical Medicine Research.* 6 (6):399–408. doi:10.14740/jocmr1905w

18. Kleint, G., Kanitz, G. & Harzer, W. 2002. Orthodontic treatment in handicapped children: report of four cases. *ASDC Journal of Dentistry for Children*. 69(1):11,31-38.

19. Knopp, C., Rudnik-Schöneborn, S., Zerres, K., Gencik, M., Spengler, S., Eggermann, T. 2015. Twenty-one years to the right diagnosis - clinical overlap of Simpson-Golabi-Behmel and Beckwith-Wiedemann syndrome. *American Journal of Medical Genetics. Part A*. 167(1):151–155. doi:10.1002/ajmg.a.36825.

20. Kobayashi, E.T., Maruyama, Y. & Kobayashi, K. 2001. A longitudinal evaluation of craniofacial growth in a patient with Kabuki Make-up syndrome: a case report. *European Journal of Orthodontics*. 23(2):205–213.

21. Koike, S., Sujino, T., Ohmori, H., Shimazaki, K., Fukuyama, E., Kanai, T., Hibi, T., Ono, T. 2013. Gastric emptying rate in subjects with malocclusion examined by [(13) C] breath test. Journal of Oral Rehabilitation. 40(8): 574–581. doi:10.1111/joor.12073

22. Mageet, A., 2016. Classification of skeletal and dental malocclusion: revisited. https://doi.org/10.25241/2016.3(2).11

23. Medeiros, P.J., Camargo, E.S., Vitral, R., Rocha, R. 2000. Orthodontic-Surgical approach in a case of severe open-bite associated with functional macroglossia. *American Journal of Orthodontics and Dentofacial Orthopedics.* 118(3):347–351. doi:10.1067/mod.2000.102390.

24. Mixter, R.C., Ewanowski, S.J. & Carson, L. V. 1993. Central tongue reduction for macroglossia. *Plastic and Reconstructive Surgery*. 91(6):1159–1162.

25. Moura, C.P., Cunha, L.M., Vilarinho, H., Cunha, M.J., Freitas, D., Palha, M., Pueschel, S.M., Pais-Clemente, M. 2008. Voice parameters in children with Down syndrome. *Journal of Voice.* 22(1):34–42. doi:10.1016/j.jvoice.2006.08.011.

26. Nargozian, C. 2004. The airway in patients with craniofacial abnormalities. *Paediatric Anaesthesia*. 14:53–59. doi:10.1046/j.1460-9592.2003.01200. x.

27. Ohshita, N., Tomiyama, Y., Iseki, A., Kawano, H., Kakuta, N., Tsutsumi, Y.M., Oshita, S.P. 2010. Anesthetic management of a child with Angelman's syndrome [Abstract]. *Masui.* 59(4):484–486.

28. Olczak-Kowalczyk, D., Witt, A., Gozdowski, D., Ginalska-Malinowska, M. 2011. Oral mucosa in children with Prader-Willi syndrome. *Journal of Oral Pathology and Medicine*. 40(10):778–784. doi:10.1111/j.1600-0714.2011.01034. x.

29. Oredugba, F.A. & Akindayomi, Y. 2008. Oral health status and treatment needs of children and young adults attending a day centre for individuals with special health care needs. *BMC Oral Health*. 8:30. doi:1472-6831-8-30.

30. Paludetti, G., Zampino, G., Della Marca, G., Di Girolamo, S., Scarano, E., Rigante, M. 2003. The tongue-base suspension using repose bone screw system in a child with Simpson-Golabi-Behmel syndrome. Case Report. *International Journal of Pediatric Otorhinolaryngology*. 67(10):1143–1147. doi:10.1016/s0165-5876(03)00220-9.

31. Purohit, B.M., Acharya, S. & Bhat, M. 2010. Oral health status and treatment needs of children attending special schools in south India: a comparative study. *Special Care in Dentistry*. 30:235–241.

32. Ribeiro, E.M., Fonteles, C.S.R., Freitas, A.B., da Silva Alves, K.S., Monteiro, A.J., da Silva, C.A.B. 2014. A clinical multicenter study of orofacial features in 26 Brazilian patients with different types of mucopolysaccharidosis. *The Cleft Palate-craniofacial Journal.* 52(3):352–358. doi:10.1597/13-204.

33. Saeves, R., Nordgarden, H., Storhaug, K., Sandvik, L., Espelid, I. 2012. Salivary flow rate and oral findings in Prader-Willi syndrome: a case-control Study. *International Journal of Paediatric Dentistry*. 22(1):27–36. doi:10.1111/j.1365-263x.2011.01153. x.

34. Sauer, C., Schlüter, B., Hinz, R., Gesch, D. 2012. Childhood obstructive sleep apnea syndrome: an interdisciplinary approach: a prospective epidemiological study of 4,318 five-and-a-half-year-old children. *Journal of Orofacial Orthopedics*. 73(5): 342–358. doi:10.1007/s00056-012-0096-x

35. Savitha, N.S, Saurabh, G., Krishnamoorthy S.H., Nandan, S., Ambili., A.2015. Hunter's syndrome: a case report. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 33(1):66-68. doi:10.4103/0970-4388.149011.

36. Scardina, G.A., Fucà, G. & Messina, P. 2007. Oral diseases in a patient affected with Prader-Willi syndrome. *European Journal of Paediatric Dentistry.* 8(2):96–99.

37. Simmons, H.C., Oxford, D.E., Hill, M.D. 2008. The prevalence of skeletal Class II patients found in a consecutive population presenting for TMD treatment compared to the national average. *The Journal of the Tennessee Dental Association*. 88 (4): 16–18.

38. Starbuck, J., Reeves, R.H. & Richtsmeier, J. 2011. Morphological integration of soft-tissue facial morphology in Down syndrome and siblings. *American Journal of Physical Anthropology*. 146(4):560–568. doi:10.1002/ajpa.21583.

39. Takahashi, M. & Ohashi, H. 2013. Craniofacial and dental malformations in Costello syndrome: a detailed evaluation using multi-detector row computed tomography. *Congenital Anomalies*. 53(2):67–72. doi:10.1111/cga.12004.

40. Thakur, A.R., Naikmasur, V.G. & Sattur, A. 2015. Hurler syndrome: orofacial, dental, and skeletal findings of a case. *Skeletal Radiology*. 44(4):579–586. doi:10.1007/s00256-014-1982-7.

41. Topouzelis, N., Iliopoulos, C. & Kolokitha, O. 2011.Macroglossia. *International Dental Journal.*61(2):63-69

42. Vellappally, S., Gardens, S.J., Al Kheraif, A.A.A., Krishna, M., Babu, S., Hashem, M., Jacob, V., Anil, S. 2014. The prevalence of malocclusion and its association with dental caries among 12-18-year-old disabled adolescents. *BMC Oral Health*. 14:123. doi:10.1186/1472-6831-14-123.

43. Vieira, G.M., Franco, E.J., da Rocha, D.F.P., de Oliveira, L.A., Amorim, R.F.B. 2015. Alternative treatment for open bite class III malocclusion in a child with Williams-Beuren syndrome. *Dental Press Journal of Orthodontics*. 20(1):97–107. doi: 10.1590/2176-9451.20.1.097-107.oar.

44. Wadenya, R.O., Stout, A.M., Gupta, A., Monge, J. 2010. Hurler syndrome: a case report of a 5-year follow-up of dental findings after bone marrow transplantation. *Special Care in Dentistry*. 30(1):14–17. doi:10.1111/j.1754-4505.2009.00115. x.

45. Williams, C. 2014. Anesthetic management of Costello syndrome: a case report. *American Association of Nurse Anesthetists*. 82(2):108–113.

46. Winter, K., Baccaglini, L. & Tomar, S. 2008. A review of malocclusion among individuals with mental and physical disabilities. *Special Care in Dentistry*.28(1): 19-26 doi:10.1111/j.1754-4505.2008.00005. x.

47. Wold, S.M., Derkay, C.S., Darrow, D.H., Proud, V. 2010. Role of the pediatric otolaryngologist in diagnosis and management of children with mucopolysaccharidoses. *International Journal of Pediatric Otorhinolaryngology*. 74(1):27–31. doi: 10.1016/j.ijporl.2009.09.042.

48. Yano, S., Baskin, B., Bagheri, A., Watanabe, Y., Moseley, K., Nishimura, A., Matsumoto, N., Ray, P.N. 2011. Familial Simpson-Golabi-Behmel syndrome: studies of X-chromosome inactivation and clinical phenotypes in two female individuals with *GPC3* mutations. *Clinical Genetics*. 80(5):466–471. doi:10.1111/j.1399-0004.2010.01554. x.

49. Yoskovitch, A., Tewfik, T.L., Brouillette, R.T., Schloss, M.D., Der Kaloustian, V.M. 1998. Acute airway obstruction in Hunter syndrome. *International Journal of Pediatric Otorhinolaryngology*. 44(3):273–278.

50. Young, W., Khan, F., Brandt, R., Savage, N., Razek, A.A., Huang, Q. 2001. Syndromes with salivary dysfunction predispose to tooth wear: case reports of congenital dysfunction of major salivary glands, Prader-Willi, Congenital Rubella, and Sjögren's syndromes. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*.92(1): 38-48.doi:10.1067/moe.2001.113549.

SECTION 3

Painting by: Ashton Paige Roberts

CHAPTER 12: DENTAL MANAGEMENT CHALLENGES IN ID

Altough only 10 participants were uncooperative during the initial screening process, the author also encountered different difficulties while meeting the dental needs of the remaining children. These included challenges with communication and behaviour as well as physical challenges.

Effective dental treatment was the ultimate aim of resolving the unmet dental needs of participants with ID and the child's ability to remain seated in the dental chair for the duration of a dental procedure played a crucial role in its success. Other influences in the long-term achievement of this goal included the participant's willingness to follow proper brushing and flossing techniques and changes in dietary behaviour. In this thesis these will be referred to as "patient compliance".

While numerous scientific articles recommend various strategies for improving patient compliance in general medicine, very few have focused on the field of dentistry. In an article addressing this issue, Macri (2015), proposed a theoretical model of motivational interviewing to encourage dental patients to improve their oral health habits. Macri's (2015) design aims to encourage patients to become actively involved in their decisions to change or enhance their dental wellbeing. Although this approach is promising and can be implemented successfully in the general population, it may not be suitable for children with ID. In particular, compliance in children with ID is affected by communication difficulties, physical challenges and behavioural problems.

12.1 Communication

During her studies, the author encountered children with varying verbal and nonverbal communication abilities. Although some children could converse confidently about issues pertaining to their day-to-day activities, they responded with uncertainty to questions posed to them about their dental habits. In other instances, children responded only when spoken to in easy sentences or when using individual words, body language or facial expressions. Others were able to understand the messages but were unable to respond effectively. The difficulties of this nature, which are challenging in several aspects of dental management, form the subject of this chapter.

12.1.1 Medical history taking

Obtaining a comprehensive medical history from children with ID is crucial for dental management. Information about underlying systemic disorders and accompanying structural problems together with the use of therapeutic agents are vital before dental intervention. In the South African context, many children are cared for by grandparents, single parents or guardians. In instances where grandparents or guardians were the primary caregivers of the children, correct medical information regarding the affected child was frequently unavailable. Also, some caregivers did not possess the ability to understand or articulate the child's condition or needs.

12.1.2 Communication with the Dentist

A large proportion of the participants were not able to verbalize the presence, source or extent of symptoms such as dental pain or discomfort. In these instances, it was difficult for the author to manage their dental needs effectively. In general, the participants involved in

the study were unable to understand fully the guidance that the author was trying to express. When simple instructions were not entirely comprehended, visual aids and gestures were utilized to gain and transfer relevant information. However, using animated language did not always elicit an appropriate response from the participants. Furthermore, it was apparent that their responses were not always an accurate reflection of their thoughts or feelings. In most instances, however, caregivers or family members assisted in facilitating communication between the child and the author.

In order to reduce anxiety and promote trust between the dentist and the participant every dental instrument was shown to the child, and its use was demonstrated in the least invasive manner. A reward system (bribery) was implemented in isolated instances.

12.1.3 Language

South Africa has eleven official languages with several dialects within the same language. The situation is complicated by the presence of immigrants from other parts of Africa speaking different languages and who are unfamiliar with indigenous tongues. Interpreters for both local and foreign languages are rarely available. In these instances, “show and tell” techniques were the only means by which the author could elicit information about the affected participant.

12.2 Behaviour

There are several reasons why children with ID behave inappropriately in the dental environment (Chaudhary, Ahlawat & Kumar, 2015). The participants in the study had varying degrees of intellectual capacity and consequently disparities in the behaviour that they expressed.

Although the association between anxiety and ID is poorly understood, it has been established that anxiety initiated by the dental environment is common and influences behaviour within the dental setting (Suprabha et al., 2011). The foundation of dental anxiety is multifactorial. Personality traits, environmental influences and cultural practices are the primary factors that determine behaviour towards dental personnel and intervention procedures (Klingberg, 2008).

During the study, the anxiety displayed by many participants may have been initiated by a negative association between pain and medical dress code, dental equipment, the dental environment. Apart from the intimidating milieu of a dental consulting room, anxiety among participants with co-morbid sensory disorders may have been amplified by bright lights, noises emitted from dental instruments, and dental materials that taste, smell and feel unfamiliar (Delli et al., 2013). Gao et al. (2013) established that dental fear among children and adolescents originated mainly from prior negative dental experiences and indirectly from negative attitudes of family members and friends. Furthermore, the majority of participants in the study were unable to understand the dental procedures, and this may have contributed to fear they experienced and the resistance they displayed to dental care (Wyne, 2002).

12.3 Behavioural management

12.3.1 Body stabilization

Inappropriate behaviour in the dental chair can interfere with the efficient provision of dental care and result in iatrogenic injuries to both the children and the dentist. A large proportion of the participants were unwilling to sit in the dental chair, while others had challenges with physical stability and difficulty maintaining balance. A minority of the participants exhibited

spontaneous body movements. In these instances, it was often necessary to steady the child's body during treatment.

Although commercially manufactured support and immobilization devices are available, a cost-efficient protocol described by Jaccarino (2009) was followed during the assessment and management at the RXH. A parent or care-giver was seated on the dental chair, and the participant positioned on the parent. The parent then gently but firmly wrapped their arms and legs around those of the participant (Fig 12.1). This method allowed a feeling of security for the participant and provided both stability and mobilization during dental procedures. Restricted movements around the chest and limbs were carefully monitored to allow for adequate circulation and breathing. When the participant experienced difficulties while being restricted, stabilization was discontinued. Informed consent from the parent or caregiver was obtained prior to any stabilization procedure.

Fig 12.1 Behavioural control protocol followed during the study.

Additional restraining techniques such as tie type arm and leg restraints and seat belt straps are mentioned in the literature. However, the author found these too invasive.

12.3.2 Mouth props

During dental procedures, a significant proportion of the children were either reluctant or unable to keep their mouths open for the dentist's access to the oral cavity. In order to maintain visibility and prevent the author from being bitten during procedures, commercially manufactured mouth props were routinely used (Fig 12.2). This device can be constructed from various inert materials.

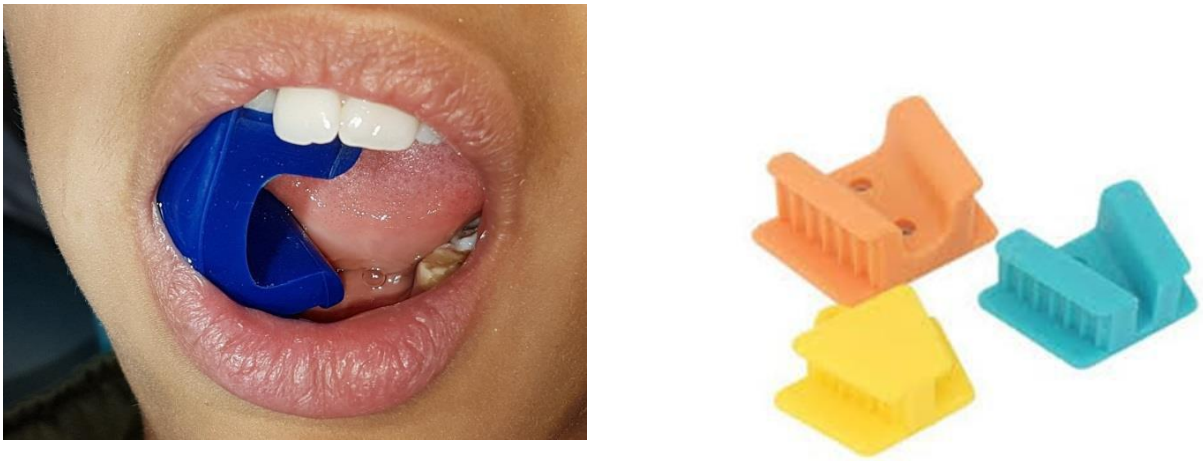


Fig 12.2 Examples of mouth props used during the investigation

When increased visibility was required at the SE Facilities, a roll of cotton gauze served to keep the mouth open during dental assessments.

Additional guidelines pertaining to the scheduling of appointments, communication and behaviour modification techniques have been proposed to ensure appropriate management within a dental facility (Nathan, 2001; Wyne, 2002; Suprabha et al., 2011; Delli et al., 2013)

12.4 Physical challenges

Apart from providing strategies to accommodate the participants' cognitive needs during dental assessment and management, it was often necessary to adapt the dental setting to offer comfort for their physical challenges. For these reasons, standard treatment protocols were modified to ensure effective dental intervention and management.

12.4.1 Short stature

The height of an individual varies between population groups and genders and it is influenced by genetic, systemic and environmental factors. Several participants with short stature (Fig 12.3) who were assessed during the survey showed signs of psychological insecurities. These concerns was extensively addressed by Whitman et al (2002) and may have contributed to the lack of compliance in the dental environment.

Fig 12.3 Short Stature: A boy aged 9 years with Coffin-Lowry syndrome standing beside a normal girl aged 7 years.

Participants with short stature often had difficulty accessing the dental chair and for this reason lowering the dental chair and providing a step stool facilitated the process. During the

survey, participants with the Hunter and Down syndromes complained about back ache that caused difficulty and discomfort during assessment and management. Physical support was provided by placing a cushion or rolled towel behind the child's lower back during dental procedures to ensure good posture and reduce pain.

Head control in the participants with short stature and unusually large heads, including those with the Hurler, Hunter and Down and syndromes, was difficult and care was exercised to prevent craniocervical instability. Limitations in neck movement also posed challenges during dental management and caution was exerted to avoid respiratory problems. This was especially challenging when treating an uncooperative participant.

Participants whose upper limbs were disproportionately short had poorer oral health than those whose body dimensions were symmetrical. This may have been the result of the limited extension of their arms leading to difficulty in reaching the the oral cavity. Similar problems were noted in participants with co-morbid motor impairment and spasticity. In these instances, the caregivers were advised and encouraged to assist the children with their routine oral healthcare at home.

The diagnoses in participants with genetic ID syndromes with accompanying short stature assessed in the survey are provided in Table XII.1. Where possible comprehensive citations from the past decade have been included.

Table XII.1: Genetic ID syndromes associated with short stature seen in the survey

Syndrome	Reference
Bardet-Biedl	Kobrin et al. 1990; Motzkin, Bianco & Zimmerman, 1992; Ozer et al. 1995; Beales et al. 1997; Riise et al. 1997; Beales et al. 1999
Coffin-Lowry	Marques Pereira et al. 2009; Nishimoto et al. 2014
Costello	Sammon et al. 2012; Anichini et al. 2013; Aytekin & Alyamac, 2013; Detweiler et al. 2013; Williams, 2014; Blachowska et al. 2016
Hunter	Neely et al. 2006; Gajula, Ramalingam & Bhadrashetty, 2012
Hurler	Ziyadeh et al., 2013
Kabuki	Tuna et al., 2012
Prader-Willi	Grugni, Sartorio & Crinò, 2016; Ludwig et al., 2016; Subbiah et al., 2016
Rubinstein-Taybi	Beets, Rodríguez-Fonseca & Hennekam, 2014; Huh et al., 2015; Kamenarova et al., 2016; de Vries et al., 2016; Karahan et al., 2016; Menke et al., 2016
Seckel	Harsha Vardhan et al., 2007
Trichorhinophalangeal	Jeon, Kim & Oh, 2014; Karaer & Yüksel, 2014; Merjaneh et al., 2014; Nagori et al., 2014; Marques et al., 2015
Williams	Bajracharya, Bhatnagar & Pauliks, 2011; Ahrens-Nicklas et al., 2015
Wolf-Hirschhorn	Roberts et al., 2009; Austin, Gunn & Jefferies, 2015

12.4.2 Tall stature

Excessive growth can be the result of endocrine and skeletal disorders. It is also a feature of a few genetic syndromes. Tall participants with genetic ID syndromes were less frequently encountered in the current survey, these included Simpson-Golabi Behmel and Sotos syndromes. Another group of participants with ID referred from the Medical Genetics Unit at RXH for dental assessment and management had marfanoid features.

12.4.3 Wheelchair-bound participants

Ideally, a dental consultation room should be equipped to accommodate patients with a variety of problems. At the RXH's dental clinic, an adequate space was available for a wheelchair to be placed beside the dental chair, and it was easy to move the majority of wheelchair-bound participants into the seat (Fig 12.4). In rare instances, where a participant was unable to be assisted into the dental chair, they were examined in the wheelchair. Unfortunately, no individual headrests were available for support, and this resulted in a somewhat compromised and extended management protocol.

Fig 12.4 A wheelchair bound boy with ID visiting the dental clinic at RXH

In ideal situations, Dougall & Fiske (2008) advocates the use of "transfer" and "banana" boards for easier relocation from wheelchairs to dental chairs (Fig 12.5).

Fig 12.5: An example of a banana board used to transfer children from wheelchairs to the dental chair

Google: https://za.pinterest.com/ (April 2017)

Customised dental units that accommodate both children in wheelchairs and general patients are commercially available (Tamazawa et al., 2004). Additional transfer devices such as hoists and portable turntables have been advocated to move patients from wheelchairs to dental chairs (Watt-Smith & Walton, 2007). In the author's survey, the majority of wheelchair bound participants were treated in the dental chair because they were often ambulant with the assistance of a caregiver.

12.4.4 Hearing impairment

Hearing impairment may be the result of pre and postnatal infection, infectious disease, traumatic birth, hereditary factors or as a component of a genetic syndrome.

The genetic ID syndromes with accompanying hearing impairment assessed in the survey are listed in Table XII.2

Table XII.2: Genetic ID syndromes associated with hearing impairment seen in the survey

Syndrome	Reference
Apert	Zhou, Schwartz & Gopen, 2009; de Jong et al., 2011; Agochukwu et al., 2014; Biamino et al., 2016
Coffin-Lowry	Hartsfield et al., 1993; Higashi & Matsuki, 1994; Rosanowski et al., 1998
Hunter	Needham et al., 2014; Tylki-Szymańska, 2014; Saurabh et al., 2015; Savitha et al., 2015; Needham et al., 2015; Parini et al., 2016; Alkhzouz et al., 2016
Hurler	Komura et al., 1998; Oghan et al., 2007; Kariya et al., 2012; Johnson, Dajnoki, & Bodamer, 2015
Kabuki	Tekin et al.,.2006; Barozzi et al., 2009; Vesseur, Cillessen & Mylanus 2016
Wolf-Hirschhorn	Lesperance et al., 1998; Ulualp et al., 2004; Battaglia, Filippi & Carey, 2008; Ahmed, Ura & Streit, 2015

Communication with the hearing-impaired participant was challenging. With mildly affected children the author spoke slowly to make a face visible for lip reading. Gestures were also

attempted to elicit positive or negative responses. Easy written messages were given to older participants who were able to read and understand. Some participants knew sign language but the author was unable to understand this method of communication in the absence of an interpreter. In some instances, visual aids assisted in conveying educational information.

12.4.5 Visual impairment

Visual deficits can range from mild impairment to the complete absence of sight. The condition can be caused by disorders affecting the eye and those that affect the areas of the brain that interpret sight. When managing the participants who had co-morbid visual impairment, it was frequently necessary to guide the participant to the dental chair. Before dental assessment or management, verbal explanations of procedures and descriptions of instruments were implemented in order to reduce anxiety. In instances where the author was required to leave the consultation area during any treatment, the reason for the absence was explained to the participant. When reentering the examination area, verbal communication was re-established. Participants with genetic ID syndromes accompanied by varying degrees of visual impairment presenting for dental management during this survey included in indviduals with Bardet-Biedl syndrome, Hurler syndrome and Oculodentodigital dysplasia.

Concluding comments:

Children with ID face several challenges with access oral heal care. Oral health professionals may encounter difficulties in communicating, establishing rapport or managing the affected childrens' behaviour. Not only will these problems increase the anxiety of the oral health care work, but it could also precipitate similar feelings in the child being treated resulting in a vicious cycle of fear and apprehension. Physical challenges such as short stature and hearing and vision impairment could complicate the practical aspects of basic dental treatment. Together the psychological and physical challenges faced by children with ID and lack of professional experience, may discourage dental practitioners to manage children with ID.

References

1. Agochukwu, N.B., Solomon, B.D. & Muenke, M. 2014. Hearing loss in syndromic craniosynostoses: introduction and consideration of mechanisms. *American Journal of Audiology*. 23(2):135–141. doi:10.1044/2014_aja-13-0036.
2. Ahmed, M., Ura, K. & Streit, A. 2015. Auditory hair cell defects as potential cause for sensorineural deafness in Wolf-Hirschhorn syndrome. *Disease Models & Mechanisms*. 8(9):1027–1035. doi:10.1242/dmm.019547.
3. Ahrens-Nicklas, R.C., Reichert, S.L., Zackai, E.H., Kaplan, P.B. 2015. Atypical Williams syndrome in an infant with complete atrioventricular canal defect. *American Journal of Medical Genetics. Part A*. 167(12):3108–3112. doi:10.1002/ajmg.a.37288.
4. Alkhzouz, C., Lazea, C., Bucerzan, S., Nascu, I., Kiss, E., Denes, C.L., Grigorescu-Sido, P. 2016. Clinical and genetic characteristics of Romanian patients with mucopolysaccharidosis type II. *JIMD Reports*. (29):1–7. doi:10.1007/8904_2016_535.
5. Anichini, C., Lotti, F., Pietrini, A., Lo Rizzo, C., Longini, M., Proietti, F., Felici, C., Buonocore, G. 2013. Antioxidant effects of potassium ascorbate with ribose in Costello syndrome. *Anticancer Research*. 33(2):691–695.
6. Austin, D.E., Gunn, A.J. & Jefferies, C.A. 2015. Severe short stature and Wolf-Hirschhorn syndrome: response to growth hormone in two cases without growth hormone deficiency. *Oxford Medical Case Reports*. 2015(2):211–214. doi:10.1093/omcr/omv008.
7. Aytekin, S. & Alyamac, G. 2013. Two new cases with Costello syndrome. *Dermatology Online Journal*. 19(8):19267.
8. Bajracharya, P., Bhatnagar, S. & Pauliks, L.B. 2011. Mitral valve diseases in Williams syndrome-case report and review of the literature. *Echocardiography*. 28(8): E156-1,9. doi:10.1111/j.1540-8175.2011.01423. x.
9. Barozzi,S., Di Berardino, F., Atzeri, F., Filipponi, E., Cerutti, M., Selicorni, A. C. 2009. Audiological and vestibular findings in the Kabuki syndrome. *American Journal of Medical Genetics, Part A.* 149(2):171–176. doi:10.1002/ajmg.a.32610.
10. Battaglia, A., Filippi, T. & Carey, J.C. 2008. Update on the clinical features and natural history of Wolf-Hirschhorn (4p-) syndrome: experience with 87 patients and recommendations for routine health supervision. *American Journal of Medical Genetics. Part C.*1 48(4):246–451. doi:10.1002/ajmg.c.30187.
11. Beales, P.L., Warner, A.M., Hitman, G.A., Thakker, R., Flinter, F.A. 1997. Bardet-Biedl syndrome: a molecular and phenotypic study of 18 families. *Journal of Medical Genetics*. 34(2):92–98.
12. Beales, P.L., Elcioglu, N., Woolf, A.S., Parker, D., Flinter, F.A. 1999. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *Journal of Medical Genetics*. 36(6):437–446.

13. Beets, L., Rodríguez-Fonseca, C. & Hennekam, R.C. 2014. Growth charts for individuals with Rubinstein-Taybi syndrome. *American Journal of Medical Genetics. Part A*. 164(9):2300–2309. doi:10.1002/ajmg.a.36654.

14. Biamino, E., Canale, A., Lacilla, M., Marinosci, A., Dagna, F., Genitori, L., Peretta, P., Silengo, M. et al. 2016. Prevention and management of hearing loss in syndromic craniosynostosis: a case series. *International Journal of Pediatric Otorhinolaryngology.* 85:95–98. doi: 10.1016/j.ijporl.2016.03.038.

15. Blachowska, E., Petriczko, E., Horodnicka-Józwa, A., Skórka, A., Pelc, M., Krajewska-Walasek, M., Walczak, M. 2016. Recombinant growth hormone therapy in a girl with Costello syndrome: a 4-year observation. *Italian Journal of Pediatrics*. 42:10. doi:10.1186/s13052-015-0209-4.

16. Chaudhary, N., Ahlawat, B. & Kumar, A. 2015. Factors affecting children' s behaviour in the dental office. *Journal of Pharmaceutical and Biomedical Sciences.* 5(12):914–918.

17. de Jong, T., Toll, M.S., de Gier, H.H.W., Mathijssen, I.M.J. 2011. Audiological profile of children and young adults with syndromic and complex craniosynostosis. *Archives of Otolaryngology-Head & Neck Surgery*. 137(8):775–778. doi:10.1001/archoto.2011.115.

18. Delli, K., Reichart, P.A., Bornstein, M.M., Livas, C. 2013. Management of children with autism spectrum disorder in the dental setting: concerns, behavioural approaches and recommendations. *Medicina Oral, Patología Oral Y Cirugía Bucal*. 18(6):e862-868.

19. Detweiler, S., Thacker, M.M., Hopkins, E., Conway, L., Gripp, K.W. 2013. Orthopedic manifestations and implications for individuals with Costello syndrome. *American Journal of Medical Genetics, Part A*. 161(8):1940–1949. doi:10.1002/ajmg.a.36047.

20. de Vries, T.I., R Monroe, G., van Belzen, M.J., van der Lans, C.A., Savelberg, S.M., Newman, W.G., van Haaften, G., Nievelstein, R.A, et al. 2016. Mosaic *CREBBP* mutation causes overlapping clinical features of Rubinstein-Taybi and Filippi syndromes. *European Journal of Human Genetics.* 24(9):1363-1366. doi:10.1038/ejhg.2016.14.

21. Dougall, A. & Fiske, J. 2008. Access to special care dentistry, Part 6. Special care dentistry services for young people. *British Dental Journal*. 205(5):235–249. doi: 10.1038/sj.bdj.2008.734.

22. Gajula, P., Ramalingam, K. & Bhadrashetty, D. 2012. A rare case of mucopolysaccharidosis: Hunter syndrome. *Journal of Natural Science, Biology, and Medicine*. 3(1):97–100. doi:10.4103/0976-9668.95984.

23. Gao, X., Hamzah, S.H., Yiu, C.K.Y., McGrath, C., King, N.M. 2013. Dental fear and anxiety in children and adolescents: qualitative study using Youtube. *Journal of Medical Internet Research*. 15(2): e29. doi:10.2196/jmir.2290.

24. Grugni, G., Sartorio, A. & Crinò, A. 2016. Growth hormone therapy for Prader-Willi syndrome: challenges and solutions. *Therapeutics and Clinical Risk Management*. 12: 873.-881.doi:10.2147/tcrm.s70068.

25. Harsha Vardhan, B.G., Muthu, M.S., Saraswathi, K., Koteeswaran D. 2007. Bird-headed dwarf of Seckel. *Journal of the Indian Society of Pedodontics and Preventative Dentistry*. 25(5):8–9.

26. Hartsfield, J.K., Hall, B.D., Grix, A.W., Kousseff, B.G., Salazar, J.F., Haufe, S.M. 1993. Pleiotropy in Coffin-Lowry syndrome: sensorineural hearing deficit and premature tooth loss as early manifestations. *American Journal of Medical Genetics*. 45(5):552–557. doi:10.1002/ajmg.1320450505.

27. Higashi, K. & Matsuki, C. 1994. Coffin-Lowry syndrome with sensorineural deafness and labyrinthine anomaly. *Journal of Laryngology and Otology*. 108(2):147–148.

28. Huh, R., Cho, S.Y., Kim, J., Ki, C.S., Jin, D.K. 2015. A novel mutation in the *CREBBP* gene of a Korean girl with Rubinstein-Taybi syndrome. *Annals of Clinical and Laboratory Science*. 45(4):458–461.

29. Jaccarino, J. 2009. general treatment considerations for the patient with special needs. *Dental Assistant*. 78:6–9, 34–36.

30. Jeon, J., Kim, J.H. & Oh, C.H. 2014. Trichorhinophalangeal syndrome Type I: clinical, microscopic, and molecular features. *Indian Journal of Dermatology, Venereology and Leprology*. 80(1):54–57. doi:10.4103/0378-6323.125515.

31. Johnson, B.A., Dajnoki, A. & Bodamer, O.A. 2015. Diagnosing lysosomal storage disorders: mucopolysaccharidosis type I. *Current Protocols in Human Genetics*. 84.17(17):1-.8. doi:10.1002/0471142905.hg1717s84.

32. Kamenarova K, Simeonov E, Tzveova R, Dacheva D, Penkov M, Kremensky I, Perenovska P, Mitev V, K.R. 2016. Identification of a novel de novo mutation of *CREBBP* in a patient with Rubinstein-Taybi syndrome by targeted next-generation sequencing: a case report. *Human Pathology.* 47(1):144–149. doi: 10.1016/j.humpath.2015.09.004.

33. Karaer, K. & Yüksel, Z. 2014. Tricho-rhino-phalangeal Syndrome type 1 as an outcome of in--vitro fertilization? *Genetic Counseling*. 25(1):13–17.

34. Karahan, M.A., Sert, H., Ayhan, Z., Ayhan, B. 2016. Anaesthetic management of children with Rubinstein-Taybi syndrome. *Turkish Journal of Anaesthesiology and Reanimation*. 44(3):152–154. doi:10.5152/tjar.2016.76992.

35. Kariya, S., Schachern, P.A., Nishizaki, K., Paparella, M.M., Cureoglu, S. 2012. Inner ear changes in mucopolysaccharidosis type I /Hurler syndrome. *Otology & Neurotology*. 33(8):1323–1327. doi: 10.1097/mao.0b013e3182659cc3.

36. Klingberg G.2008. Dental anxiety and behaviour management problems in paediatric dentistry: a review of the background factors and diagnostics. *European Archives of Paediatric Dentistry.*9(Suppl 1):11-15

37. Kobrin, J.L., Ternand, C.L., Knobloch, W.H., Johnson, D.D. 1990. Dental abnormalities as a component of the Laurence-Moon-Bardet-Biedl syndrome. *Ophthalmic Paediatrics and Genetics*. 11(4):299–303.

38. Komura Y, Kaga K, Ogawa Y, Yamaguchi Y, Tsuzuku T, S.J. 1998. ABR and temporal bone pathology in Hurler's disease. *Internal Journal of Pediatric Otorhinolaryngology*. 43(2):179–188.

39. Lesperance, M.M., Grundfast, K.M., Rosenbaum, K.N. 1998. Otologic manifestations of Wolf-Hirschhorn syndrome. *Archives of Otolaryngology--Head & Neck Surgery*. 124(2):193–196.

40. Ludwig, N.G., Radaeli, R.F., Silva, M.M.X., Romero, C.M., Carrilho, A.J.F., Bessa, D., Macedo, D.B., Oliveira, M.L., et al. 2016. A boy with Prader-Willi syndrome: unmasking precocious puberty during growth hormone replacement therapy. *Archives of Endocrinology and Metabolism*. 60(6):596–600. doi:10.1590/2359-3997000000196.

41. Macri, D. V. 2015. stratergies for improving patient compliance. *Dimensions of Dental Hygiene*. 13(12):27–29.

42. Marques, J.S., Maia, C., Almeida, R., Isidoro, L., Dias, C. 2015. should patients with Trichorhinophalangeal syndrome be tested for growth hormone deficiency? *Pediatric Endocrinology Reviews*. 13(1):465–467.

43. Marques Pereira, P., Schneider, A., Pannetier, S., Heron, D., Hanauer, A. 2009. Coffin–Lowry Syndrome. *European Journal of Human Genetics*. 18(6):627–633. doi:10.1038/ejhg.2009.189.

44. Menke, L.A., van Belzen, M.J., Alders, M., Cristofoli, F., DDD Study, Ehmke, N., Fergelot, P., Foster, A., et al. 2016. *CREBBP* mutations in individuals without Rubinstein-Taybi syndrome phenotype. *American Journal of Medical Genetics. Part A*. Part A. 170(10): 2681–2693.doi:10.1002/ajmg.a.37800.

45. Merjaneh, L., Parks, J.S., Muir, A.B. & Fadoju, D. 2014. A novel *TRPS1* gene mutation causing Trichorhinophalangeal syndrome with growth hormone responsive short stature: a case report and review of the literature. *International Journal of Pediatric Endocrinology*. 2014(1):16. doi:10.1186/1687-9856-2014-16.

46. Motzkin, N.E., Bianco, A.J. & Zimmerman, D. 1992. Tibia vara in a patient with Bardet-Biedl syndrome. *Mayo Clinic Proceedings*. 67(6):549–552.

47. Nagori, S.A., Jose, A., Agarwal, B., Bhatt, K., Bhutia, O., Roychoudhury, A. 2014. Traumatic bone cyst of the mandible in Langer-Giedion syndrome: a case report. *Journal of Medical Case Reports*. 8:387. doi:10.1186/1752-1947-8-387.

48. Nathan, J.E. 2001. Behavioral management strategies for young pediatric dental patients with disabilities. *ASDC Journal of Dentistry for Children*. 68(2):89–101.

49. Needham, M., Packman, W., Rappoport, M., Quinn, N., Cordova, M., Macias, S., Morgan, C., Packman, S. 2014. MPS II: adaptive behavior of patients and impact on the family system. *Journal of Genetic Counseling*. 23(3):330–338. doi:10.1007/s10897-013-9665-4.

50. Needham, M., Packman, W., Quinn, N., Rappoport, M., Aoki, C., Bostrom, A., Cordova, M., Macias, S., et al. 2015. Health-Related quality of life in patients with MPS II. *Journal of Genetic Counseling*. 24(4):635–644. doi:10.1007/s10897-014-9791-7.

51. Neely, J., Carpenter, J., Hsu, W., Jordan, L., Restrepo, L. 2006. Cerebral infarction in Hunter syndrome. *Journal of Clinical Neuroscience.* 13(10):1054–1057. doi: 10.1016/j.jocn.2005.12.038.

52. Nishimoto, H.K., Ha, K., Jones, J.R., Dwivedi, A., Cho, H.M., Layman, L.C., Kim, H.G. 2014. The historical Coffin-Lowry syndrome family revisited: identification of two novel mutations of *RPS6KA3* in three male patients. *American Journal of Medical Genetics.Part A*. 164(9):2172–2179. doi:10.1002/ajmg.a.36488.

53. Oghan, F., Harputluoglu, U., Guclu, E., Guvey, A., Turan, N., Ozturk, O. 2007. Permanent T-tube insertion in two patients with Hurler's syndrome. *International Journal of Audiology*. 46(2):94–96. doi:10.1080/14992020600975287.

54. Ozer, G., Yüksel, B., Süleymanova, D., Alhan, E., Demircan, N. & Onenli, N. 1995. clinical features of Bardet-Biedl syndrome. *Acta Paediatrica Japonica.*37(2):233–6.

55. Parini, R., Jones, S.A., Harmatz, P.R., Giugliani, R., M.N. 2016. The natural history of growth in patients with Hunter syndrome: data from the Hunter Outcome Survey (HOS). *Molecular Genetic Metabolsim.* 117(4):438–446. doi: 10.1016/j.ymgme.2016.01.009.

56. Puri, S., Bhattarai, D., Adhikari, P., Shrestha, J.B., Paudel, N. 2015. Burden of ocular and visual disorders among pupils in special schools in Nepal. *Archives of Disease in Childhood*. 100(9):834–837. doi:10.1136/archdischild-2014-308131.

57. Riise, R., Andréasson, S., Borgaström, M.K., Wright, A.F., Tommerup, N., Rosenberg, T., Tornqvist, K. 1997. Intrafamilial variation of the phenotype in Bardet-Biedl syndrome. *British Journal of Ophthalmology*. 81(5):378–385.

58. Roberts, T., Stephen, L.X.G., Fieggen, K., Beighton, P. 2009. Wolf-Hirschhorn syndrome; oro-dental manifestations and management. *Journal of Clinical Pediatric Dentistry*. 34(2):173–176.

59. Rosanowski, F., Hoppe, U., Proschel, U., Eysholdt, U. 1998. Late-onset sensorineural hearing loss in Coffin-Lowry syndrome. *Journal for Oto-Rhino-Laryngology and Its Related Specialties*. 60(4):224–226.

60. Sammon, M.R., Doyle, D., Hopkins, E., Sol-Church, K., Stabley, D.L., McGready, J., Schulze, K., Alade, Y., et al. 2012. Normative growth charts for individuals with Costello syndrome. *American Journal of Medical Genetics. Part A*. 158A (11):2692–2699. doi:10.1002/ajmg.a.35534.

61. Savitha, N.S., Saurabh, G., Krishnamoorthy, S.H., Nandan, S. & Ambili, A. 2015. Hunter's syndrome: a case report. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 33(1):66–68. doi:10.4103/0970-4388.149011 [doi].

62. Subbiah, S., Chinnathurai, R., Sangumani, J., Somasundaram, S. 2016. A rare association of obesity, diabetes mellitus and bilateral cryptorchidism: Prader - Willi syndrome. *Journal of the Association of Physicians of India*. 64(11):97–98.

63. Suprabha, B.S., Rao, A., Choudhary, S., Shenoy, R. 2011. Child dental fear and behavior: the role of environmental factors in a hospital cohort. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 29(2):95–101. doi:10.4103/0970-4388.84679.

64. Tamazawa, Y., Watanabe, M., Kikuchi, M., Takatsu, M., Tamazawa, K., Yumoto, N., Hyvarinen, P. 2004. A new dental unit for both patients in wheelchairs and general patients. *Gerodontology*. 21(1):53–59.

65. Tekin M, Fitoz S, Arici S, Cetinkaya E, I.A. 2006. Niikawa-Kuroki (Kabuki) syndrome with congenital sensorineural deafness: evidence for a wide spectrum of inner ear abnormalities. *International Journal of Pediatriac Otorhinolaryngology.* 70(5):885–889. doi: 10.1016/j.ijporl.2005.09.025.

66. Tuna, E.B., Marşan, G., Gençay, K., Seymen, F. 2012. Craniofacial and dental characteristics of Kabuki Syndrome: nine years cephalometric follow-up. *Journal of Clinical Pediatric Dentistry*. 36(4):393–400.

67. Tylki-Szymańska, A. 2014. Mucopolysaccharidosis type II, Hunter's syndrome. *Pediatric Endocrinology Reviews*. 12:107–113. doi:10.1001/archderm.102.5.578.

68. Ulualp, S.O., Wright, C.G., Pawlowski, K.S., Roland, P.S. 2004. Histopathological basis of hearing impairment in Wolf-Hirschhorn syndrome. *The Laryngoscope*. 114(8):1426–1430. doi:10.1097/00005537-200408000-00021.

69. Vesseur, A., Cillessen,E & Mylanus, E. 2016. Cochlear Implantation in a patient with Kabuki syndrome. *Journal of International Advanced Otology*. 12(1):129–131. doi:10.5152/iao.2016.2004.

70. Watt-Smith, P. & Walton, G. 2007. A case study on the use of turntable transfer. *Journal of Disability & Oral Health*. 8(3):132–134.

71. Whitman, B.Y., Myers, S., Carrel, A., Allen, D. 2002. The behavioral impact of growth hormone treatment for children and adolescents with Prader-Willi syndrome: a 2-year, controlled study. *Pediatrics*. 109(2):E35. Available at: http://pediatrics.aappublications.org/content/109/2/e35

72. Williams, C. 2014. Anesthetic management of Costello syndrome: a case report. *American Association of Nurse Anesthetists*. 82(2):108–113.

73. Wyne, A. 2002. Dental management of mentally retarded patients. *Pakistan Oral & Dental Journal.* 22(1). Available at: http://www.podj.com.pk/PODJ/Vol.%2022%20(1)%20(June%202002)/22_1_03-08.pdf

74. Zhou, G., Schwartz, L.T. & Gopen, Q. 2009. Inner ear anomalies and conductive hearing loss in children with Apert syndrome: an overlooked otologic aspect. *Otology & Neurotology.* 30(2):184–189. doi:10.1097/mao. ob013e318191a352.

75. Ziyadeh J, Merrer, L., Robert, M., Arnaud, E., Valayannopoulos, V., Di Rocco, F. 2013. Mucopolysaccharidosis type 1 and craniosynostosis. *Acta Neurochirurgica*. 155(10):1973–1976. doi:10.1007/s00701-013-1831-9.

CHAPTER 13: SYSTEMIC CONSIDERATIONS IN DENTAL MANAGEMENT OF CHILDREN WITH ID

Introduction

In this study, several participants with genetic ID syndromes also had underlying systemic abnormalities. These complications were variable and either occurred secondary to the intellectual disability or were syndromic components. Irrespective of the type or aetiology of the disorder the author took responsibility for the holistic management of the participants while in her care. In doing so, she was required to have a sound knowledge of the syndromic associations that accompany several well-known genetic ID syndromes. The conditions in these categories, their effects on the oral cavity and the dental management considerations that apply to these disorders are documented and discussed in this chapter.

13.1 Congenital Cardiac Defects

Congenital heart defects (CHD) are present in approximately 1% of live births in the USA and South Africa (De Decker & van der Merwe, 2011; Krasuski et al., 2016). Common CHDs in children with genetic ID syndromes include septal defects and valvular insufficiencies. There is a higher prevalence of poor oral hygiene in children with congenital heart disease (Tasioula, Balmer & Parsons, 2008; Hegde et al., 2012). Several factors including unfavourable social circumstances, the chronic use of medication and inadequate dietary habits may contribute to oral disorders such as gingivitis and dental caries among these children.

The eleven genetic and chromosomal ID syndromes accompanied by cardiac abnormalities which were encountered in the study are listed in Table XIII.1. The references which are

quoted pertain to articles published since the begining of 2012 in which the dental aspects of these conditions are documented and discussed.

Table XIII.1: Genetic ID syndromes associated with cardiovascular defects encountered in the survey

Syndrome	Reference
Bardet-Biedl	Andersson et al., 2013; Ferreira do Amaral et al., 2014; Suspitsin & Imyanitov, 2016
Coffin-Lowry	Norderyd & Aronsson, 2012
Costello	Takahashi & Ohashi, 2013; Goodwin et al., 2014
Down	Jones & Morrison, 2016; Limeres Posse et al., 2016; Singh, Bhatia & Sharma, 2017; van der Linden et al., 2017
Hunter	Saurabh et al., 2015; Khan et al., 2017
Hurler	McGovern et al., 2010; Thakur, Naikmasur & Sattur, 2015
Kabuki	Tuna et al., 2012; Saurabh et al., 2015
Seckel	Arora, Rattan & Ghai, 2012; Ramalingam et al., 2012
Turner	Evlice et al., 2013; Pentinpuro, Lähdesmäki & Alvesalo, 2013; Pentinpuro et al., 2014; Nakayama et al., 2015
Williams	Cogulu, Hazan & Dindaroglu, 2015; Wong, Ramachandra & Singh, 2015; Torres et al., 2015; Vieira et al., 2015
Wolf-Hirschhorn	Dellavia et al., 2011; Paradowska-Stolarz, 2014

The viridans group of streptococci which includes the most virulent strain of cariogenic bacteria, *Streptococcus mutans,* have been implicated as important aetiological agents in the development of infective endocarditis (Nobbs, 2017). Accordingly, the presence of untreated dental caries poses a risk of bacteraemia and is a potential initiator of this complication. In the current survey, it is relevant that there was a high prevalence of dental caries in the participants at both the SE Facilities and the RXH.

Although the study did not specifically investigate the way in which cardiac disease correlates with the prevalence of dental caries in the participants, it seems likely that children with a combination of ID, cardiac defects and extensive carious lesions may be at a greater risk of developing infective endocarditis.

A document promulgated by the American Heart Association (AHA) (2016) stated that they do not recognize an association between periodontal pathogens and cardiovascular disease. Nevertheless, Ziebolz et al. (2015) had previously reported the discovery of bacterial DNA originating from the oral cavity and inflammatory markers in the myocardial tissue of persons with aortic valve stenosis. These findings suggest a possible relationship between periodontal bacteria and valvular heart disease.

In the author's study, the screening techniques were limited to the detection of gingival disease. While this condition is reversible in most instances, there are occasions in which gingival disease may progress to periodontitis. The precise pathogenic mechanism responsible for the progression of chronic gingivitis to active periodontitis is unclear, but the status of the host's defence mechanism and the organism's virulence are crucial factors (Hasan & Palmer, 2014).

It is the author's experience that the prevalence of gingival disease in the participants attending the SE Facilities (69%) and at the RXH (86%) was high. Based on the observations of Zieboltz et al. (2015) and the immune impairment of several participants in the study, it is possible that these children could be at risk of developing infective valvular disease.

13.1.1 Dental management implications

When participants with a history of a cardiac defect were referred for dental management, their physician was contacted in order to establish the type and extent of the heart condition

prior to treatment. Care was taken to ensure that no invasive measures were implemented without the consent of the practitioner.

The AHA have published guidelines for the prophylactic use of antibiotics in dentistry (American Heart Association, 2016) but this protocol has not been uniformly implemented in South Africa. In the context of the author's study, and when deemed appropriate, prophylactic antibiotics were administered one hour before dental procedures that had the potential to introduce bacteria into the bloodstream.

13.2 Hypertension

Systemic hypertension occurs in certain genetic ID disorders notably, the Williams and Bardet-Biedl syndromes. When the author was presented with hypertensive participants with these conditions, the child's blood pressure (BP) was measured prior to dental procedures at every visit and all values were documented. On occasions where the BP was elevated, the appointment was postponed, and the participant referred for medical attention. Apart from elevated BPs, factors such as the duration, invasiveness, urgency of dental procedures as well as the general health of the child warranted consideration in the management of the participant.

13.2.1 Dental implications

Several mucosal conditions are associated with hypertension including gingival haemorrhage and gingival hyperplasia, xerostomia, lichenoid drug eruptions and facial nerve palsy (Kumar et al., 2012).

13.2.2 Dental management implications

The use of local anaesthetics (LAs) which contain vasoconstrictive substances for individuals with hypertension is contentious. During the investigations LAs without vasoconstrictors was administered prior to invasive dental procedures to participants with elevated blood pressure. Knoll-Köhler et al. (1989) reported that the level of endogenous catecholamines increases more than 40-fold during stressful periods and cautioned against the use of vasoconstrictors. Conversely, Serrera Figallo et al. (2012) reported no contraindications for LA containing epinephrine in persons with controlled hypertension. Children with ID are often anxious, and when suffering from painful episodes (for example, toothache) their levels of stress are amplified. In these circumstances excessive amounts of endogenous vasoactive compounds may be released from their adrenal glands. This sequence of events may result in a hypertensive crisis, although this outcome is rare in dental practice.

In the wider dental context of LA, it is relevant that epinephrine is metabolised rapidly and has several beneficial effects. These include decreased blood flow to anaesthetized areas during dental procedures and intensification of the quality and degree of anaesthesia. In non-ID children who present with unusual bleeding tendencies, low doses of LA with epinephrine are administered for complicated procedures. In the study, when a parent or care-giver of a hypertensive participant gave a history of abnormally long periods of bleeding after an extraction, the amount of LA was restricted. When additional anaesthesia was required, a LA without epinephrine was used, and multiple procedures involving different areas of the mouth were avoided. The use of epinephrine is given further consideration in chapter 15.

13.3 Respiratory Disorders

Severe congenital and genetic abnormalities in the dentoalveolar area can compromise respiration. These include clefts of the lip and or palate, microstomia and midface hypoplasia. Similarly, breathing can be impaired by skeletal abnormalities such as a small thorax and spinal malalignment. These complications have important implications for dental management under sedation and are discussed in chapter 14.

13.4 Epileptic Seizures

Epileptic seizures result from sudden, electrical emissions from the brain resulting in changes in behaviour, spontaneous movement or consciousness. Seizures are either “partial” (when the electrical discharge can be localized to a specific area of the cortex) or “generalized” (when discharges are emitted from the entire brain). Epileptic seizures have multiple aetiologies and can accompany certain genetic ID syndromes. A sudden seizure during a dental procedure could harm both the child and the dentist. In particular, a sudden jerk or movement could displace sharp instruments such as a dentist’s drill or probe and cause severe damage to oral tissue and aspiration of dental material. Furthermore, a tightened jaw together with a posteriorly displaced tongue could compromise the airway and result in aspiration. During management of participants with a history of epilepsy and/or seizure disorders, the author remained aware of signs and symptoms of the potential development of an epileptic episode.

13.4.1 Dental implications

Persons using some form of antiepileptic medication for continued periods may develop thrombocytopenia, vertigo, lethargy, and headache. The dental consequences include xerostomia, increased likelihood of microbial infections, delayed wound healing, and unwarranted bleeding (Joshi et al., 2013). Together with an impaired intellectual capacity, these may give rise to gingivitis and dental caries.

13.4.2 Dental management implications

In order to manage a participant experiencing a seizure it was necessary for the author to know the difference between a seizure, a vasovagal episode caused by a lowered oxygen level, and apparent hypoglycaemia. Familiarity with the management protocol of these medical emergencies was essential. If a seizure occurred, the initial response was to protect the participant's airway, avoid restraining the child if possible and administer high flow oxygen. If the seizure lasted for 5 minutes or more (status epilepticus), medication was administered via the intravenous route.

The specific genetic conditions in which epileptic seizures are a syndromic component and were encountered in the survey are listed in Table XIII.2. Relevant references from the dental literature were also tabulated.

Table XIII.2: Genetic ID syndromes associated with epileptic seizures encountered in the survey

Syndrome	Reference
Angelman	Murakami et al. 2008; Sarkar et al. 2011; Gallo et al. 2012; Margolis et al. 2015
Apert	Martelli et al. 2008
Coffin-Lowry	Marques Pereira et al. 2009; Hahn and Hanauer 2012; Nishimoto et al. 2014; Imataka et al. 2016
Incontinentia Pigmenti	Kitakawa et al. 2009; Meuwissen and Mancini 2012; Margari et al. 2013; Pizzamiglio et al. 2014; Wolf et al. 2015
Hunter	Saurabh et al. 2015
Hurler	Thomas & Tandon 2000
Kabuki	Lodi et al. 2010; Yoshioka et al. 2011; Verrotti et al. 2011; Sobral et al. 2013; Sattur et al. 2014
Sotos	Hirai et al. 2011; Nicita et al. 2012
Wolf-Hirschhorn	Roberts et al. 2009; Dellavia et al. 2011; Paradowska-Stolarz 2014; Zollino et al. 2014

13.5 Diabetes Mellitus

The American Diabetes Association (2009) has defined Diabetes Mellitus (DM) as "a group of metabolic disorders in which both genetic and environmental conditions may contribute to the aetiology". The prevalence of insulin-dependent and Type-2 diabetes is currently higher than in the past and varies between geographical areas. Children with ID syndromes are more likely to develop DM than non-ID children (Taggart, Coates & Truesdale-Kennedy, 2013). In the current study, participants with the Turner, Prader-Willi, Bardet-Biedl, Down and Candle syndromes had DM.

13.5.1 Dental implications

Hyperglycemia, a key feature of DM, can cause multiorgan damage and may influence the initiation and progression of oral disorders such as periodontitis. Indeed, periodontal disease is more common in children with DM than in the general population (Novotna et al., 2015). Moreover, the systemic infection and inflammation caused by periodontal pathogens has an adverse effect on the control of hyperglycaemia and may influence the complications of DM (Taylor & Borgnakke, 2008). Diabetes Mellitus may also contribute to dental caries, burning mouth syndrome, salivary dysfunction/xerostomia, taste and other neurosensory disorders, altered tooth eruption and benign parotid hypertrophy (Albert et al., 2012).

3.5.2 Dental management implications

Additional oral problems in DM include delayed healing after invasive procedures such as extractions and an increased susceptibility to opportunistic infections such as Candidiasis.

Concluding comments:

It is relevant that systemic disorders may accompany ID and impact upon the oral tissues. Moreover, the medication used to control or manage these disorders may have adverse effects on both the hard and soft tissues of the oral cavity. Furthermore, certain systemic disorders including congenital cardiac defects, respiratory abnormalities, DM, hypertension and epileptic seizures that may accompany ID, have management implications for children being treated in the dental office and under general anaesthesia.

For this reason, a sound knowledge of general medicine and pharmacology is required due to the potential presence of a variety of systemic disorders which may impact on the dental management of children with ID.

References

1. Albert, D. A., Ward, A., Allweiss, P., Graves, D.T., Knowler, W.C., Kunzel, C., Leibel, R.L., Novak, K.F., et al. 2012. Diabetes and oral disease: implications for health professionals. *Annals of the New York Academy of Sciences*. 1255:1–15. doi:10.1111/j.1749-6632.2011.06460. x.

2. American Diabetes Association. 2009. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 32(Suppl. 1):62-67. doi:10.2337/dc09-s062.

3. American Heart Association. 2016. *Antibiotic Prophylaxis Prior to Dental Procedures*. Available: http://www.ada.org/en/member-center/oral-health-topics/antibiotic-prophylaxis.

4. Andersson, E.M., Axelsson, S., Gjølstad, L.F., Storhaug, K. 2013. Taurodontism: a minor diagnostic criterion in Laurence-Moon/Bardet-Biedl syndromes. *Acta Odontologica Scandinavica*. 71(6):1671–1674. doi:10.3109/00016357.2013.794389.

5. Arora, S., Rattan, V. & Ghai, B. 2012. Anesthetic management of a child with Seckel syndrome for multiple extractions and restoration of teeth. *Journal of Anaesthesiology Clinical Pharmacology*. 28(3):398-299. doi:10.4103/0970-9185.98361.

6. Cogulu, D., Hazan, F. & Dindaroglu, F.C. 2015. Orofacial findings and dental management of Williams syndrome. *Genetic Counseling*. 26(4):437–442.

7. De Decker, R. & van der Merwe, E. 2011. Managing congenital heart disease and comorbidities - opening a pandora's box? *Continuing Medical Education*. 29(11/12):456. Available at: <http://www.cmej.org.za/index.php/cmej/article/view/2284/2049>.

8. Dellavia, C., Raiteri, S., Ottolina, P., Pregliasco, F. 2011. Oral features in five adult patients with Wolf-Hirschhorn syndrome. *Minerva Stomatologica*. 60(7–8):391–402.

9. do Prado Sobral, S., Leite, A.F., Figueiredo, P.T.S., Ferrari, Í., Safatle, H.P.N., Córdoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013. Craniofacial and dental features in Kabuki syndrome patients. *The Cleft Palate-Craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.

10. Evlice, B., Tatli, U., Yazicioglu, I., Evlice, A., Oztunc, H. 2013. A unique case of Turner syndrome accompanying prolactinoma and unexpected elongated styloid process: clinical and cone-beam computed tomographic features. *Imaging Science in Dentistry*. 43(2):129-134. doi:10.5624/isd.2013.43.2.129.

11. Ferreira do Amaral, C.O., Logar, Gde A., Parisi, A.G., Takahashi, K., Straioto, F.G. 2014. General and stomatologic aspects of Bardet-Biedl syndrome. *Journal of Craniofacial Surgery*. 25(6): e575–e578. doi:10.1097/scs.0000000000001169.

12. Gallo, C., Marcato, A., Beghetto, M., Stellini, E. 2012. Dental treatment in Angelman Syndrome patients. 8 case reports. *European Journal of Paediatric Dentistry.* 13(4):345–348.

13. Goodwin, A.F., Oberoi, S., Landan, M., Charles, C., Massie, J.C., Fairley, C., Rauen, K.A., Klein, O.D. 2014. Craniofacial and dental development in Costello syndrome. *American Journal of Medical Genetics Part A*. 164(6):1425–1430. doi:10.1002/ajmg.a.36475.

14. Hahn, J.S. & Hanauer, A. 2012. Stimulus-induced drop episodes in Coffin-Lowry syndrome. *European Journal of Medical Genetics*. 55(5):335–337. doi: 10.1016/j.ejmg.2012.03.004.

15. Hasan, A. & Palmer, R.M. 2014. A clinical guide to periodontology: pathology of periodontal disease. *British Dental Journal*. 216(8):457–461. doi: 10.1038/sj.bdj.2014.299.

16. Hegde, A.M., Kavita, R., Sushma, K.S., Suchetha, S. 2012. Salivary sialic acid levels and dental health in children with congenital heart disease. *Journal of Clinical Pediatric Dentistry*. 36(3):293–296.

17. Hirai, N., Matsune, K. & Ohashi, H. 2011. Craniofacial and oral features of Sotos syndrome: differences in patients with submicroscopic deletion and mutation of *NSD1* gene. *American Journal of Medical Genetics.Part A*. 155(12):2933–2939. doi:10.1002/ajmg.a.33969.

18. Imataka, G., Nakajima, I., Goto, K., Konno, W., Hirabayashi, H., Arisaka, O. 2016. Drop episodes improved after tracheotomy: a case of Coffin-Lowry syndrome associated with obstructive sleep apnea syndrome. *European Review for Medical and Pharmacological Sciences*. 20(3):498–501.

19. Jones, D. & Morrison, J. 2016. Preventative therapies and periodontal interventions for Down syndrome patients. *Evidence-Based Dentistry*. 17(4):101–102. doi: 10.1038/sj.ebd.6401198.

20. Joshi, S.R., Pendyala, G.S., Saraf, V., Choudhari, S., Mopagar, V., 2013. A comprehensive oral and dental management of an epileptic and intellectually deteriorated adolescent. *Dental Research Journal.* 10(4): 562–567.

21. Khan, M.A., Addison, O., James, A., Hendriksz, C.J., Al-Jawad, M. 2017. Synchrotron X-ray diffraction to understand crystallographic texture of enamel affected by Hunter syndrome. *Archives of Oral Biology*. 80:193–196. doi: 10.1016/j.archoralbio.2017.04.019.

22. Kitakawa, D., Fontes, P.C., Magalhães, F.A.C., Almeida, J.D., Cabral, L.A.G. 2009. Incontinentia pigmenti presenting as hypodontia in a 3-year-old girl: a case report. *Journal of Medical Case Reports*. 3:116. doi:10.1186/1752-1947-3-116.

23. Knoll-Köhler, E., Frie, A., Becker, J., Ohlendorf, D. 1989. Changes in plasma epinephrine concentration after dental infiltration anesthesia with different doses of epinephrine. *Journal of Dental Research*. 68(6):1098–1101.

24. Krasuski, R.A., Bashore, T.M., Warnes, C., Williams, R., Bashore, T., Child, J., Connolly, H., Dearani, J., et al. 2016. Congenital heart disease epidemiology in the United States: blindly feeling for the charging elephant. *Circulation*. 134(2):110–113. doi:10.1161/circulationaha.116.023370.

25. Kumar, P., Mastan, K.M.K., Chowdhary, R., Shanmugam, K., 2012. Oral manifestations in hypertensive patients: A clinical study. *Journal of Oral Maxillofacial Pathology.* 16(2): 215. doi.10.4103/0973-029X.99069

26. Limeres Posse, J., López Jiménez, J., Ruiz Villandiego, J.C., Cutando Soriano, A., Fernández Feijoo, J., Linazasoro Elorza, M., Diniz Freitas, M., Diz Dios, P. 2016. Survival of dental implants in patients with Down syndrome: a case Series. *Journal of Prosthetic Dentistry*. 116(6):880–884. doi: 10.1016/j.prosdent.2016.04.015.

27. Lodi, M., Chifari, R., Parazzini, C., Viri, M., Beccaria, F., Lorenzetti, M.E., Meloni, M., Capovilla, G., et al. 2010. Seizures and EEG pattern in Kabuki syndrome. *Brain & Development*. 32(10):829–834. doi: 10.1016/j.braindev.2009.12.006.

28. Margari, L., Lamanna, A.L., Buttiglione, M., Craig, F., Petruzzelli, M.G., Terenzio, V. 2013. Long-term follow-up of neurological manifestations in a boy with Incontinentia pigmenti. *European Journal of Pediatrics*. 172(9):1259–1262. doi:10.1007/s00431-013-2021-8.

29. Margolis, S.S., Sell, G.L., Zbinden, M.A., Bird, L.M. 2015. Angelman Syndrome. *Neurotherapeutic.* 12(3):641–650. doi:10.1007/s13311-015-0361-y.

30. Marques Pereira, P., Schneider, A., Pannetier, S., Heron, D., Hanauer, A. 2009. Coffin–Lowry syndrome. *European Journal of Human Genetics*. 18(6):627–633. doi:10.1038/ejhg.2009.189.

31. Martelli, H., Paranaíba, L.M.R., de Miranda, R.T., Orsi, J., Coletta, R.D. 2008. Apert syndrome: report of a case with emphasis on craniofacial and genetic features. *Pediatric Dentistry*. 30(6):464–468.

32. McGovern, E., Owens, L., Nunn, J., Bolas, A., Meara, A. & Fleming, P. 2010. Oral features and dental health in Hurler syndrome following hematopoietic stem cell transplantation *International Journal of Paediatric Dentistry*. 20(5):322–329. doi:10.1111/j.1365-263x.2010.01055. x.

33. Meuwissen, M.E.C. & Mancini, G.M.S. 2012. Neurological findings in Incontinentia pigmenti; a review. *European Journal of Medical Genetics*. 55(5):323–331. doi: 10.1016/j.ejmg.2012.04.007.

34. Murakami, C., Nahas Pires Correa, M.S., Nahas Pires Correa, F., Nahas Pires Correa, J.P. 2008. Dental treatment of children with Angelman syndrome: a case report. *Special Care in Dentistry.* 28(1):8–11. doi:10.1111/j.1754-4505.2008.00003. x.

35. Nakayama, M., Lähdesmäki, R., Niinimaa, A., Alvesalo, L. 2015. Molar morphology and the expression of carabelli's trait in 45X females. *American Journal of Human Biology*. 27(4):486–493. doi:10.1002/ajhb.22674.

36. Nicita, F., Ruggieri, M., Polizzi, A., Mauceri, L., Salpietro, V., Briuglia, S., Papetti, L., Ursitti, F., et al. 2012. Seizures and epilepsy in Sotos syndrome: analysis of 19 caucasian patients with long-term follow-up. *Epilepsia*. 53(6): e102-e105. doi:10.1111/j.1528-1167.2012.03418. x.

37. Nishimoto, H.K., Ha, K., Jones, J.R., Dwivedi, A., Cho, H.M., Layman, L.C., Kim, H.G. 2014. The historical Coffin-Lowry syndrome family revisited: identification of two novel mutations of *RPS6KA3* in three male patients. *American Journal of Medical Genetics.Part A*. 164(9):2172–2179. doi:10.1002/ajmg.a.36488.

38. Nobbs, A. 2017. Getting to the heart of the matter: role of *Streptococcus Mutans* adhesin cnm in systemic disease. *Virulence*. 8(1):1-4. doi:10.1080/21505594.2016.1212157.

39. Norderyd, J. & Aronsson, J. 2012. Hypoplastic root cementum and premature loss of primary teeth in Coffin-Lowry syndrome: a case report. *International Journal of Paediatric Dentistry*. 22(2):154–156. doi:10.1111/j.1365-263x.2011.01160. x.

40. Novotna, M., Podzimek, S., Broukal, Z., Lencova, E., Duskova, J. 2015.Periodontal diseases and dental caries in children with type 1 Diabetes Mellitus. *Mediators of Inflammation*. 2015:1-8. doi:10.1155/2015/379626.

41. Paradowska-Stolarz, A.M. 2014. Wolf-Hirschhorn Syndrome (WHS) - Literature review on the features of the syndrome. *Advances in Clinical and Experimental Medicine*. 23(3):485–489.

42. Pentinpuro, R.H., Lähdesmäki, R.E. & Alvesalo, L.J. 2013. Root lengths in the permanent teeth of 45X females. *Acta Odontologica Scandinavica*. 71(3–4):778–785. doi:10.3109/00016357.2012.734399.

43. Pentinpuro, R.H., Lähdesmäki, R.E., Niinimaa, A.O., Pesonen, P.R.O., Alvesalo, L.J. 2014. Crown heights in the permanent teeth of 45X And 45X/46XX females. *Acta Odontologica Scandinavica*. 72(8):908–916. doi:10.3109/00016357.2014.921327.

44. Pizzamiglio, M.R., Piccardi, L., Bianchini, F., Canzano, L., Palermo, L., Fusco, F., D'Antuono, G., Gelmini, C., et al. 2014. Incontinentia pigmenti: learning disabilities are a fundamental hallmark of the disease. *PLoS ONE*. 9(1). e87771. Availabe at: https://doi.org/10.1371/journal.pone.0087771 doi: 10.1371/journal.pone.0087771.

45. Ramalingam, K., Kaliyamurthy, S., Govindarajan, M., Swathi, S. 2012. Seckel syndrome: a report of a case. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 30(3):258-261. doi:10.4103/0970-4388.105021.

46. Roberts, T., Stephen, L.X.G., Fieggen, K., Beighton, P. 2009. Wolf-Hirschhorn syndrome; oro-dental manifestations and management. *The Journal of Clinical Pediatric Dentistry*. 34(2):173–176.

47. Roberts, T., Stephen, L., & Beighton, P., 2013. Cleidocranial dysplasia: a review of the dental, historical, and practical implications with an overview of the South African experience. *Oral Surgery. Oral Medicine Oral Pathology. Oral Radiology.* 115(1): 46–55.doi.10.1016/j.oooo.2012.07.435

48. Sarkar, P.A., Shigli, A. & Patidar, C. 2011. Happy Puppet syndrome. *BMJ Case Reports*. 2011. 2011: bcr0920114747. doi:10.1136/bcr.09.2011.4747.

49. Sattur, A., Deshmukh, P.K., Abrahim, L. & Naikmasur, V.G. 2014. Kabuki Make-up syndrome - a case report with electromyographic study. *Journal of Clinical and Diagnostic Research.* 8(11):ZD03-6. doi:10.7860/jcdr/2014/9804.5122.

50. Saurabh, G., Krishnamoorthy, S., Nandan, S., Ambili, A., Savitha, N. 2015. Hunter's Syndrome: a case report. *Journal of Indian Society of Pedodontics and Preventive Dentistry*.33(1): 66.doi:10.4103/0970-4388.149011.

51. Serrera Figallo, M., Velázquez Cayón, R., Lagares, D.T., Corcuera Flores, J.R., Portillo, G.M. 2012.Use of anesthetics associated to vasoconstrictors for dentistry in patients with cardiopathies. *Journal of Clinical and Experimental Dentistry*. 4(2):107–111.doi:10.4317/jced.50590.

52. Singh, A., Bhatia, H.P. & Sharma, N. 2017. Coexistence of fusion and concrescence of primary teeth: in a child with Down syndrome. *Special Care in Dentistry*. 37(3):147–149.doi:10.1111/scd.12218.

53. Sobral, S.D.P., Leite, A.F., Figueiredo, P.T.S., Ferrari, I., Safatle, H.P.N., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013.Craniofacial and dental features in Kabuki Syndrome patients. *Cleft Palate-craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.

54. Suspitsin, E.N. & Imyanitov, E.N. 2016. Bardet-Biedl Syndrome. *Molecular Syndromology*. 7(2):62–71.doi:10.1159/000445491.

55. Taggart, L., Coates, V. & Truesdale-Kennedy, M. 2013. Management and quality indicators of Diabetes Mellitus in people with intellectual disabilities. *Journal of Intellectual Disability Research.*57(12):1152–1163. doi:10.1111/j.1365-2788.2012.01633. x.

56. Takahashi, M. & Ohashi, H. 2013.Craniofacial and dental malformations in Costello syndrome: a detailed evaluation using multi-detector row computed tomography. *Congenital Anomalies*.53(2):67–72.doi:10.1111/cga.12004.

57. Tasioula, V., Balmer, R. & Parsons, J.2008.Dental health and treatment in a group of children with congenital heart disease. *Pediatric Dentistry*. 30(4):323–328.

58. Taylor, G.W. & Borgnakke, W.S. 2008.Periodontal disease: associations with diabetes, glycemic control and complications. *Oral Diseases*. 14(3):191–203. doi:10.1111/j.1601-0825.2008.01442. x.

59. Thakur, A.R., Naikmasur, V.G. & Sattur, A. 2015.Hurler syndrome: orofacial, dental, and skeletal findings of a case. *Skeletal Radiology*. 44(4):579–586. doi:10.1007/s00256-014-1982-7.

60. Thomas, S. & Tandon, S. 2000.Hurler syndrome: a case Report. *The Journal of Clinical Pediatric Dentistry*. 24(4):335–338.

61. Torres, C.P., Valadares, G., Martins, M.I., Borsatto, M.C., Díaz-Serrano, K.V., de Queiroz, A.M. 2015. Oral findings and dental treatment in a child with Williams-Beuren syndrome. *Brazilian Dental Journal*. 26(3):312–316. doi:10.1590/0103-6440201300335.

62. Tuna, E.B., Marşan, G., Gençay, K., Seymen, F. 2012.Craniofacial and dental characteristics of Kabuki syndrome: nine years cephalometric follow-up. *The Journal of Clinical Pediatric Dentistry*.36(4):393–400.

63. van der Linden, M.S., Vucic, S., van Marrewijk, D.J.F., Ongkosuwito, E.M. 2017. Dental development in Down syndrome and healthy children: a comparative study using the Demirjian method. *Orthodontics & Craniofacial Research*. 20(2):65–70. doi:10.1111/ocr.12139.

64. Verrotti, A., Agostinelli, S., Cirillo, C., D'Egidio, C., Mohn, A., Boncimino, A., Coppola, G., Spalice, A., et al. 2011.Long-term outcome of epilepsy in Kabuki syndrome. *Seizure*. 20(8):650–654.doi: 10.1016/j.seizure.2011.06.005.

65. Vieira, G.M., Franco, E.J., Rocha, D.F.P. da Oliveira, L.A. & de Amorim, R.F.B. 2015. Alternative treatment for open bite class III malocclusion in a child with Williams-Beuren syndrome. Dental *Press Journal of Orthodontics*.20(1):97–107.doi: 10.1590/2176-9451.20.1.097-107.oar.

66. Wolf, D.S., Golden, W.C., Hoover-Fong, J., Applegate, C., Cohen, B.A., Germain-Lee, E.L., Goldberg, M.F., Crawford, T.O., et al. 2015. High-dose glucocorticoid therapy in the management of seizures in neonatal Incontinentia pigmenti: a case report. *Journal of Child Neurology*. 30(1):100–106.doi:10.1177/0883073813517509.

67. Wong, D., Ramachandra, S. & Singh, A. 2015. Dental Management of patient with Williams syndrome - a case report. *Contemporary Clinical Dentistry*. 6(3):418-420. doi:10.4103/0976-237x.161908.

68. Yoshioka, S., Takano, T., Matsuwake, K., Sokoda, T. & Takeuchi, Y. 2011. A Japanese patient with Kabuki syndrome and unilateral perisylvian cortical dysplasia. *Brain & Development*. 33(2):174–6. doi: 10.1016/j.braindev.2010.04.001.

69. Ziebolz, D., Rost, C., Schmidt, J., Waldmann-Beushausen, R., Schondube, F.A., Mausberg, R.F. & Danner, B.C. 2015. Periodontal bacterial DNA and their link to human cardiac tissue: findings of a pilot study. *Thoracic and Cardiovascular Surgeon*. doi:10.1055/s-0035-1564689.

70. Zollino, M., Orteschi, D., Ruiter, M., Pfundt, R., Steindl, K., Cafiero, C., Ricciardi, S., Contaldo, I., et al. 2014. Unusual *4p16.3* deletions suggest an additional chromosome region for the Wolf-Hirschhorn syndrome-associated seizures disorder. *Epilepsia*. 55(6):849–857. doi:10.1111/epi.12617.

CHAPTER 14: HUMAN IMMUNODEFICIENCY VIRUS AND ACQUIRED IMMUNODEFICIENCY SYNDROME

Infection with the Human Immunodeficiency Virus (HIV) and the subsequent Acquired Immunodeficiency Syndrome (AIDS) is a pandemic immunodeficiency disease characterized by overwhelming immunosuppression. The disease is associated with opportunistic infections, secondary neoplasms and neurologic changes. The human immunodeficiency viruses (HIV) types 1 and 2 are the primary causative organisms of AIDS and are transmitted via several routes including sexual intercourse, contaminated needles and/or syringes, recipient blood products and donated organs. The most common transmission pathway of the HIV in children is from an infected mother to her child before, during or after birth and while breastfeeding (UNAIDS, 2010). Transmission through sexual exposure of an unaffected child to an infected individual sometimes takes place in South Africa.

The Joint United Nations Programme on HIV and AIDS (UNAIDS, 2014) have estimated that between 6 700 000 - 7 400 000 people in South Africa are either infected with HIV or living with AIDS (Fig 14.1). Of these persons, approximately 4 000 000 are women of childbearing age. These figures indicate that South Africa has the world's largest HIV and AIDS epidemic (UNICEF, 2016). Figure XIV.1 illustrates the estimated global prevalence of HIV and AIDS among adolescents and young adults in 2016.

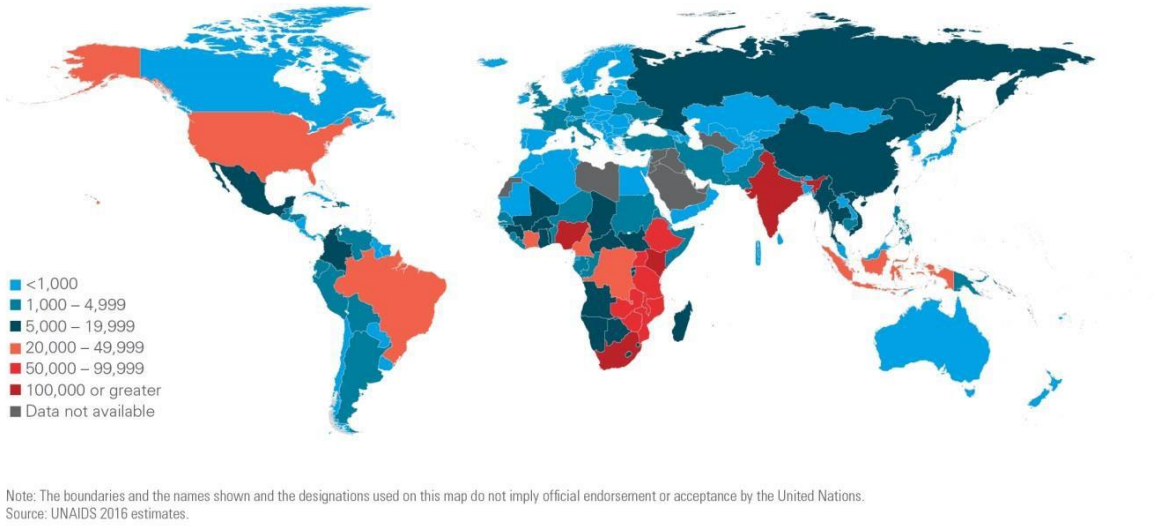


Fig 14.1 Global prevelance of HIV and AIDS among adolescents and young adults

Source: https://data.unicef.org/ (April 2017)

Despite their greater exposure to exploitation and abuse, the documented prevalence of HIV and AIDS amongst children with ID is incomplete and no data are currently available from Sub-Saharan Africa in this regard (Merrick et al., 2010). In these circumstances and given the high prevalence of HIV and AIDS among South African women and children, the author deemed it pertinent to discuss this disorder and the dental complications as they were very relevant to the study.

14.1 Clinical Spectrum HIV Infection

The early phase of the disease usually manifests as an acute infection and is present in approximately 10-20 percent of infected individuals. The initial clinical symptoms include a sever sore throat, cervical lymphadenopathy, fever, malaise, fatigue, enlarged tonsils, headache and painful muscles. These features may mimick glandular fever and typically

precede seroconversion. Neurological signs such as aseptic meningitis, encephalopathy and neuropathy may accompany this phase of the disease.

The latent or chronic illness may be asymptomatic and last between 2 and 10 years. The most common feature of this phase is persistent generalised lymphadenopathy (GL) comprising of enlarged nodes in two or more extra-inguinal sites and occurs in the absence of any other cause of lymphadenopathy. The final phase of infection is divided into two categories namely, the AIDS-related complex and full-blown AIDS. Diarrhoea, night sweats, weight loss and oral candidiasis are features commonly encountered in patients with AIDs –related complex and full-blown AIDS. The latter is usually accompanied by opportunistic infections, tumours and neurologic disease.

Although candidiasis (Fig 14.2) is the most common oral feature of HIV and AIDS, other lesions occur in the oral cavity. These differ between geographic locations, age groups and the levels of CD4 lymphocytes.

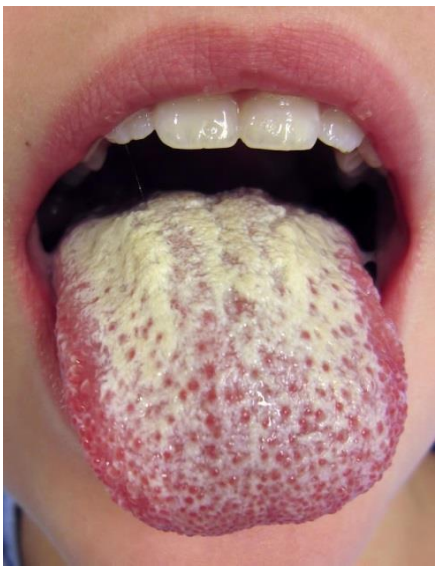


Fig 14.2 Candidal infection of the tongue commonly seen in HIV positive children and adults.

Source: https://en.wikipedia.org/ (April 2017)

During early childhood development infection with the Human Immunodeficiency Virus (HIV) may directly influence the developing brain resulting in cognitive impairment. Factors such as inadequate nutrition, the absence of intellectual stimulation and adverse socioeconomic circumstances may compound this problem (Huston et al., 1994; Ravindran et al., 2014).

It is likely that a significant proportion of the South African population infected with HIV/AIDS have either not been tested for or are oblivious of their status. Furthermore, some individuals may be unwilling to disclose their HIV status to a dental practitioner. For these reasons, the author undertook her project with the assumption that all children in the study were HIV positive. This approach was in alignment with the UWC Faculty of Dentistry's protocol for infection control (chapter 3).

14.2 HIV\AIDS and the Oral Cavity

HIV can present with specific changes to both the hard and soft tissues of the oral cavity. For these reasons, it is possible to conclude that factors such as these may have had an influence on the findings in the project.

Angular cheilitis (Fig XIV.2) and pseudomembranous candidiasis (Fig XI.3) are common mucocutanesous lesions which often occur in HIV infected children with CD 4 counts less than 500.

Since the widespread therapeutic use of highly active antiretroviral therapy (HAART) the incidence and development of certain oral lesions associated with HIV such as oral hairy leukoplakia, Kaposi's sarcoma, and necrotizing periodontitis have decreased. Others, namely human papillomavirus infections and caries, have increased in adults (Peacock, Arce & Cutler, 2017). The effect of HAART on the oral structures of children remain contentious. Sales-Peres (2012) reported different types of oral lesions found in HIV positive children taking HAART

compared to those not on HAART therapy. Conversely, Jose et al. (2013) noted no significant difference in the oral lesions between the two groups.

Although the oral manifestations of HIV in children in the general population are well documented, there are no scientific reports describing oro-dental lesions in children with a combination of ID and HIV. In the general population, the reported prevalence of oral diseases amongst all children with HIV in the lower socioeconomic levels ranges from between 53% and 73 % overseas (Rwenyonyi et al., 2011; Oyedeji et al., 2015) and between 45% and 63% in South Africa (Naidoo and Chikte 2004).

Periodontal disease (PD) is one of the most common oral complications of HIV and AIDS. None of the children in the current study had clinical evidence of PD and the environment in which the research was conducted precluded investigation procedures for its detection. However, less severe forms of periodontal changes may accompany HIV infection. These include necrotising gingivitis and linear erythematous gingivitis. In the study, 69% of children attending the SE Facilities and 86% at the RXH presented with gingival disease. These values are significantly higher than those for similarly aged children affected by HIV described by Flaitz et al. (2001) who reported gingival disease in only 9% of children with HIV infection.

The prevalence of dental caries among children living with HIV and AIDS is dependent upon the age group of the child. In early childhood, the reported frequency varies between 5O % and 59% in younger children and between 30% and 77% in older children (Beena, 2011; Masiga and M'Imunya, 2013). In the current study, the frequency of dental caries was consistently high among all the children irrespective of age in those seen at the RXH and gradually increased with age amongst those attending the SE Facilities.

Apart from dental caries, enamel hypoplasia is reported to be one of the most frequent problems affecting the teeth of children with HIV. The frequency of the disorder ranges between approximately 23% and 45% (Magalhães et al., 2001; Oyedeji et al., 2015). Irrespective of this limitation, their reported findings are higher than those recorded in the author's investigation (7.5% and 38% at the SE Facilities and the RXH respectively).

References

1. Beena, J.P. 2011. Prevalence of dental caries and its correlation with the immunologic profile in HIV-infected children on antiretroviral therapy. *European Journal of Paediatric Dentistry*. 12(2):87–90.
2. Flaitz, C., Wullbrandt, B., Sexton, J., Bourdon, T., Hicks, J. 2001. Prevalence of orodental findings in HIV-infected Romanian children. *Pediatric Dentistry*. 23(1):44–50.
3. Huston, A.C., McLoyd, V.C. & Coll, C.G. 1994. Children and poverty: issues in contemporary research. *Child Development*. 65(2):275–282. doi:10.1111/1467-8624.ep9405315099.
4. Jose, R., Chandra, S., Puttabuddi, J.H., Vellappally, S., Al Khuraif, A.A.A., Halawany, H.S., Abraham, N.B., Jacob, V., et al. 2013. Prevalence of oral and systemic manifestations in pediatric HIV cohorts with and without drug therapy. *Current HIV Research*. 11(6):498–505.
5. Magalhães, M.G., Bueno, D.F., Serra, E., Gonçalves, R. 2001. Oral Manifestations of HIV positive children. Journal *of Clinical Pediatric Dentistry*. 25(2):103–106.
6. Masiga, M.A. & M'Imunya, J.M. 2013. Prevalence of dental caries and its impact on quality of life (QoL) among HIV-infected children in Kenya. *Journal of Clinical Pediatric Dentistry*. 38(1):83–87.
7. Merrick, J., Talnir, R., Gross, S., Chemtob, D., Aspler, S., Kandel, I., Morad, M. 2010. Human Immunodeficiency Virus (HIV) and persons with disability / intellectual disability: a review. *International Public Health Journal*. 2(3):285–288.
8. Naidoo, S. & Chikte, U. 2004. Oro-facial Manifestations in paediatric HIV: a comparative study of institutionalized and hospital outpatients. *Oral Diseases*. 10(1):13–18. doi:10.1046/j.1354-523x.2003.00973. x.
9. Oyedeji, O.A., Gbolahan, O.O., Oluwatoyin Abe, E., Agelebe, E. 2015. Oral and dental lesions in HIV infected Nigerian children. *Pan African Medical Journal*. 20:287. doi:10.11604/pamj.2015.20.287.5273.
10. Peacock, M.E., Arce, R.M. & Cutler, C.W. 2017. Periodontal and other oral manifestations of immunodeficiency diseases. *Oral Diseases*.23(7):866-888. doi:10.1111/odi.12584.
11. Ravindran, O.S., Rani, M.P. & Priya, G. 2014. Cognitive deficits in HIV infected children. *Indian Journal of Psychological Medicine*. 36(3):255–259. doi:10.4103/0253-7176.135373.
12. Rwenyonyi, C.M., Kutesa, A., Muwazi, L., Okullo, I., Kasangaki, A., Kekitinwa, A. 2011. Oral manifestations in HIV/AIDS-infected children. *European Journal of Dentistry*. 5(3):291–298.
13. Sales-peres, S.H.D.C. 2012. Oral manifestations in HIV + children in Mozambique. *Ciencia & Saude Coletiva*. 17(1):55–60. doi:10.1590/s1413-81232012000100008.
14. UNAIDS. 2010. *UNAIDS Global report 2010 | UNAIDS Report on the Global AIDS Epidemic 2010*. Available at: http://www.unaids.org/globalreport/Global_report.htm

15. UNAIDS. 2014. *South Africa | UNAIDS/. (2014):2014–2015*. Available at: http://www.unaids.org/en/regionscountries/countries/southafrica

16. UNICEF. 2016. *UNICEF Eastern and Southern Africa - HIV and AIDS – Overview.* Available at: https://www.unicef.org/esaro/5482_HIV_AIDS.html

CHAPTER 15: MEDICATION IN THE DENTAL MANAGEMENT OF ID

Introduction

Medicinal therapy is an important component of dental practice and the potential complications and management issues are reviewed in this section.

In South Africa, dental practitioners are permitted to prescribe scheduled medication. It is relevant that any drug used or administered in the dental setting may result in adverse reactions. For example, antibiotics routinely prescribed for the alleviation of oral infections could predispose children to oral fungal infections. Similarly, medicines prescribed by the general medical practitioners to control epilepsy and manage cardiac disorders may induce oral changes such as gingival hypertrophy.

15.1. Drug Interactions

The simultaneous use of one or more drugs could give rise to unfavourable chemical interactions and toxicity. These problems often arise from the interplay between constituents of the drug, factors affecting the host and hypersensitivity reactions to a pharmacological compound.

During this study, the author remained vigilant about any systemic disorders in the participants and paid particular attention to the medication prescribed by their general medical practitioners. A comprehensive medical history was undertaken for each participant prior to any dental treatment. She also updated her knowledge of the pharmacological actions and potential drug interactions relevant to medications taken by the children.

Potential drug interactions while treating participants with underlying systemic conditions include the following:

15.1.1 Haemorrhage

The interaction of several groups of drugs may increase the risk of bleeding in dental practice. Non-steroidal anti-inflammatory medicines (NSAIDS), are commonly advocated for use with acute and chronic pain but can increase the possibility of haemorrhage when used in conjunction with selective serotonin reuptake and protein pump inhibitors (Picksak et al. 2010; Wallace et al. 2011; Dawoud et al. 2014; Verhaegh et al. 2016). This phenomenon can also arise with the simultaneous ingestion of antifungal agents, such as metronidazole, and anticoagulant agents (Kovac, Mitic & Kovac, 2012; Mohan, 2016).

15.1.2 Changes in Drug Efficacy

The concurrent use of two or more drugs may interfere with the efficacy of either or both of them. These interactions may either be synergistic, antagonistic or may induce a new effect (Dawoud, Roberts & Yates, 2014). The intensity and severity of their interactions may vary from being inconspicuous to potentially life threatening. Drugs such as NSAIDs, routinely prescribed by a dental practitioner to alleviate dental pain, when used concurrently with antihypertensive medication such as ACE inhibitors, beta-blockers and diuretics, may reduce their efficacy. Furthermore, the simultaneous use of macrolide amides such as erythromycin, routinely prescribed for oral bacterial infections, can potentiate and prolong the hypotensive effects of calcium channel blockers (Wright et al., 2011; Henneman & Thornby, 2012; Bucsa et al., 2015). According to the literature, the simultaneous use of simvastatin and macrolide antibiotics or azole antifungals may result in muscle toxicity (Hamilton-Craig, 2001).

15.2 Local Anaesthetics

Local anaesthetics (LA) are commonly administered to alleviate pain in dentistry. The primary function of a LA agent is to induce temporary anaesthesia at the site of application or injection. This result is accomplished by substances derived from either aminoamide or aminoester compounds. Additional substances such as vasoconstrictors, preservatives, reducing agents and isotonic vehicles may also be present in LA solutions.

Although the use of LAs is safe at therapeutic doses, these drugs may have both local and systemic adverse effects in high-risk individuals.

15.2.1 Adverse Reactions to LA Agents

Overdose and Toxicity

High doses of LA can occur in the bloodstream following injection of a LA. Apart from an excessive volume of the drug being introduced into the vascular system, several risk factors can also contribute to an overdose. These include standard doses delivered to underweight children, especially those with genetic syndromes and growth impairment (chapter13) and in individuals with liver and kidney dysfunction. When disorders of the liver are present, the LA might fail to metabolise adequately, while in children with renal disorders insufficient drug elimination could occur.

Drug overdose and toxicity are more common in children with liver damage or liver dysfunction. In children with ID, liver impairment may develop as a component of a genetic syndrome or may follow an environmental insult. Syndromic liver disease is rare but sporadic instances have been reported in children with Kabuki syndrome (Nobili et al., 2004) and Tuberous Sclerosis (Kechaou et al. 2014). Irrespective of the cause, children with liver

dysfunction have an increased risk of maintaining high levels of LA in their bloodstream which may ultimately lead to toxicity (Singh, 2013).

Hypersensitivity reactions

The most common hypersensitivity reactions to LA agents are acute allergic reactions via IgE-mediated pathways and those that are mediated via T cell responses, namely, Type–IV or delayed hypersensitivity reactions. In general, delayed Type-IV hypersensitivity is associated with ester-based LAs and occurs more frequently than IgE-mediated reactions (Caballero, Tsabouri & Dugue, 2009).

Type-IV immunological responses to LAs can result from both sensitization to an LA agent or cross-reactions between different LAs compounds. When they occur in the oral cavity, the reaction can present clinically as a swelling or contact dermatitis at the site of application (Caballero, Tsabouri & Dugue, 2009). Benzocaine, an esther-based LA, is a common ingredient of topical anaesthetics and induces sensitization in susceptible individuals, while cocaine and tetracaine may cross-react with each other (Finucane, 2003).

15.3 Vasoconstrictors: epinephrine (chapter 12)

Both amide- and ester-based LAs cause vasodilation and if not controlled this can result in high levels of these agents in the bloodstream. Epinephrine, a widely used vasoconstrictor, is routinely added to LA solutions to decrease the blood flow and increase the time of exposure of the LA to the nerve consequently minimising the risk of toxicity, decreasing bleeding and prolonging the duration of action of the LA at the site of application. These vasoconstrictors increase the heart rate, stimulate the brain, increase certain metabolic functions, constrict blood vessels and inhibit the action of the muscles around the bronchi and the gastrointestinal tract. The adverse effects of vasoconstrictors are fundamentally associated

with excessive dosages and the introduction of the substances directly into the bloodstream (Cassidy, Phero & Grau, 1986).

The sympathetic effect of epinephrine in LA can be potentiated by the concurrent administration of tricyclic antidepressants and non-selective cardio-beta blockers. This combination can result in palpitations, tachycardia, arrhythmia, anxiety, headache, tremor, and hypertension.

Concluding comments:

None of the children displayed any adverse drug reactions during the study. However, the author continued to remain vigilant of the possible negative consequences associated with the use of routinely prescribed medication in the participants and particularly in those with comorbid systemic conditions. The participant's medical condition was regularly reviewed and caution was exercised when prescribing medication to alleviate pain, treat oral infections and using LA.

References:

1. Bucsa, C., Moga, D.C., Farcas, A., Mogosan, C., Dumitrascu, D.L. 2015. An investigation of the concomitant use of angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and diuretics. *European Review for Medical and Pharmacological Sciences*. 19(15):2938–2944.
2. Caballero, M.R., Tsabouri, S. & Dugue, P. 2009. Hypersensitivity to local anaesthetics - 6 facts and 7 myths. *Current Allergy and Clinical Immunology*. 22(3):117–120.
3. Cassidy, J.P., Phero, J.C. & Grau, W.H. 1986. Epinephrine: systemic effects and varying concentrations in local anesthesia. *Anesthesia Progress*. 33(6):289–297.
4. Dawoud, B.E.S., Roberts, A. & Yates, J.M. 2014. Drug interactions in general dental practice - considerations for the dental practitioner. *British Dental Journal*. 216(1):15–23. doi: 10.1038/sj.bdj.2013.1237.
5. Finucane, B.T. 2003. Allergies to local anesthetics - the real truth. *Canadian Journal of Anaesthesia*. 50(9):869–874. doi:10.1007/bf03018730.
6. Hamilton-Craig, I. 2001. Statin-associated myopathy. *Medical Journal of Australia*. 175(9): 486-489.doi:10.1001/jama.289.13.1681.
7. Henneman, A. & Thornby, K.A. 2012. Risk of hypotension with concomitant use of calcium-channel blockers and macrolide antibiotics. *American Journal of Health-System Pharmacy*. 69(12):1038–1043. doi:10.2146/ajhp110486.
8. Kechaou, I., Cherif, E., Ben Hassine, L., Khalfallah, N. 2014. Liver involvement in tuberous sclerosis. *BMJ Case Reports*. doi:10.1136/bcr-2013-201650.
9. Kovac, M., Mitic, G. & Kovac, Z. 2012. Miconazole and nystatin used as topical antifungal drugs interact equally strongly with warfarin. *Journal of Clinical Pharmacy and Therapeutics*. 37(1):45–48. doi:10.1111/j.1365-2710.2011.01246. x.
10. Mohan, S. 2016. Prime drug interplay in dental practice. *Journal of Clinical and Diagnostic Research*. 10(3): ZE07–ZE11. doi:10.7860/jcdr/2016/16912.7434.
11. Nobili, V., Marcellini, M., Devito, R., Capolino, R., Viola, L., Digilio, M.C. 2004. Hepatic fibrosis in Kabuki syndrome. *American Journal of Medical Genetics. Part A*. 124(2):209–212. doi:10.1002/ajmg.a.20387.
12. Picksak, G., Höner zu Siederdissen, C. & Stichtenoth, D.O. 2010. SSRI-associated bleeding risk. [Abstract]. *Medizinische Monatsschrift Fur Pharmazeuten*. 33:217–218.
13. Singh, P. 2013. Systemic toxicity of local anesthetics: a point to ponder. *Toxicology International.*20(2):194. Doi:10.4103/0971-6580.117273
14. Verhaegh, B.P.M., de Vries, F., Masclee, A.A.M., Keshavarzian, A., de Boer, A., Souverein, P.C., Pierik, M.J., Jonkers, D.M.A.E. 2016. High risk of drug-induced microscopic colitis with concomitant use of NSAIDS and proton pump inhibitors. *Alimentary Pharmacology & Therapeutics*. 43(9):1004–1013. doi:10.1111/apt.13583.
15. Wallace, J.L., Syer, S., Denou, E., De Palma, G., Vong, L., McKnight, W., Jury, J., Bolla, M., et al. 2011. Proton pump inhibitors exacerbate NSAID-induced small intestinal injury by inducing dysbiosis. *Gastroenterology*. 141(4):1314–1322.e5 doi: 10.1053/j.gastro.2011.06.075.

16. Wright, A.J., Gomes,T., Mamdani,M.M.,, Horn, J.R., Juurlink, D.N. 2011. The risk of hypotension following co-prescription of macrolide antibiotics and calcium-channel blockers. *Canadian Medical Association Journal*. 183(3):303–307.

CHAPTER 16: GENERAL ANAESTHESIA IN THE DENTAL MANAGEMENT OF CHILDREN WITH ID

Many dental procedures among children in the general population are completed in the dental chair. However, in some instances the lack of cooperation, high frequency of anxiety and comorbid craniofacial abnormalities amongst the participants necessitated specific sedation methods during the study. Additionally, children requiring extensive procedures and those with uncontrollable behaviour or sensory or physical problems were also considered for dental management under sedation. However, these strategies were only contemplated after the implementation of several behavioural modification techniques. The sedation regimes employed during this study were general anaesthesia (GA) and conscious sedation. The management of the participants using general anaesthesia is outlined and discussed in this chapter in the light of the author's experience during the investigation.

16.1 Patient selection

The selection of participants for dental treatment under GA as opposed to alternative sedation techniques was based on their general health, behaviour and level of movement and followed the protocol compiled by the UWC Faculty of Dentistry was followed (annexure 5). Before undergoing GA, individual participants were evaluated by a physician to establish whether they were medically suitable for the planned procedures to be undertaken.

A high level of cooperation and the least possible undesirable patient movement is necessary to avoid unnecessary iatrogenic trauma or aspiration of dental material during dental treatment. For these reasons the participants' demeanour and extent of movement in the dental setting were assessed by a Frankl Behaviour scale (Table XVI.1) and the

modified Houpt scale (Table XVI.2). The Frankl scale categorizes a child's observed behaviour in the dental chair and is a useful tool for planning future clinical visits. The Houpt scale allowed the author to evaluate compliance in the dental chair.

Table XVI.1: Frankl Behavioural Rating Scale (modified)

Group	Behaviour
1	Completely uncooperative
2	Relatively uncooperative
3	Accepts treatment with caution. Attempts compliance with dentist.
4	No resistance to treatment. Accepts treatment

Source: (AMERICAN ACADEMY OF PEDIATRIC Dentistry, 2011)

Table XVI.2: Houpt scale for evaluating the inappropriate movement by children (modified**)**

Category	Movement
1	Violent movement constantly interrupting examination
2	Constant movement that hinders examination
3	Controllable movements that do not interfere with the procedure
4	Lack of movement

Source: (Houpt et al., 1985))

The participants involved in this investigation who required dental intervention under GA were managed either in the general operating theatres at the RXH or in the Faculty of Dentistry, Tygerberg Hospital (TGH). The times allocated at the RXH for dental procedures were limited, and only participants without concomitant medical conditions requiring extractions and those needing tooth restorations in their permanent dentition were treated

under GA at this facility. For this reason, the majority of the participants were referred to the dental faculty at TGH. This hospital is equipped with theatres and employ the services of skilled theatre staff and a medically qualified anesthesiologist. During the preoperative procedure phase the advantages and disadvantages of GA were given consideration. Relevant points are listed below.

16.2 Advantages of GA in managing participants with ID

- GA is a safe, efficient and convenient technique for treating a patient who is unable to be managed in the dental consulting rooms
- Multiple procedures may be performed in during one session
- Minimal or no patient compliance is necessary
- No emotional trauma is inflicted on the patient
- The throat pack placed in the patient's airway prevents the aspiration of debris

16.3 Disadvantages of GA when managing children with ID

- Compared to other forms of sedation, GA has an increased risk of complications especially in children with ID. These problems may occur during and after procedures and include depression of the cardiovascular and respiratory systems. For these reasons, and where possible, routine dental treatment under local anaesthesia was preferred.
- Since the risks accompanying dental procedures under GA are significant, laboratory tests, chest radiography and electrocardiography were necessary in some instances. These investigations were often difficult to complete due to excessive anxiety and noncompliance and required extra time and expense.

- Specialized training, equipment and facilities were needed and an anaesthesitic team was essential.
- There were several technical challenges during GA procedures. These included:
    - The dentist's vision was obstructed during the introduction of the intubation tube
    - The anaesthetized participant lacked voluntary movement, which, in some instances resulted in difficulty in accessing the mouth. In addition, this immobility affected the dentist's posture.
    - The cost of all the procedures was high.

16.4 Preoperative GA procedures

The author explained the procedures to the child's parent(s) or primary care-giver before all dental treatment under GA. This process included a detailed explanation of the risks, benefits and alternative measures (where possible). After the author was satisfied that the parent(s)/primary caregiver understood the processes, written consent was obtained.

Preoperative assessment

The author documented a comprehensive medical history during each participant's initial dental visit and presented it to the anaesthetist before the GA. Information such as the particular cause of ID, comorbid systemic conditions, craniofacial and skeletal malformations, medication, past operations, and allergies was detailed. Where possible, any history of difficult intubations and postoperative complications were recorded.

16.5 Local Analgesia during GA

In the preoperative procedure discussion, the issue of local anaesthesia was addressed. Despite the fact that the participants could not feel pain during GA procedures, local anaesthesia could be used to control postoperative pain and reduce bleeding. The route of local analgesia might differ from child to child and depended on the type and extent of the dental treatment. In instances where minor intervention of short duration was foreseen, infiltration anaesthesia using 2% lidocaine and 1/80,000 adrenalin solution would be injected. More extensive procedures or those requiring extended periods of time would necessitate regional anaesthesia such as inferior alveolar nerve blocks.

Closing comment:

Patient compliance is important for the effective dental management of children with ID. Sudden movements or misbehaviour in the dental chair may displace instruments and cause significant harm. For this reason, general anaesthesia or conscious sedation techniques were employed to provide optimal dental treatment in the shortest period of time. Careful patient selection and assessment was a primary concern. Furthermore, the advantages and disadvantages of a particular mode of sedation was considered prior to dental procedures.

References:

1. American Academy of Pediatric Dentistry, 2011. Guideline on behavior guidance for the pediatric patient: *American Academy of Pediatric Dentistry reference manual.* 36, 179–191.
2. Houpt, M.I., Sheskin, R.B., Koenigsberg, S.R., Desjardins, P.J., Shey, Z., 1985. Assessing chloral hydrate dosage for young children. *ASDC Journal of Dentistry for Children.* 52 (5): 364–369.

CHAPTER 17: CHALLENGES DURING THE GENERAL ANAESTHESIA IN CHILDREN WITH ID

Introduction

The challenges faced before and during dental treatment under GA by the participants, the dentist and the anaesthetist are discussed in this chapter.

17.1 Challenges visualising the larynx

Any factor affecting both the soft and hard tissue of the dentofacial complex and airway may influence the intubation process. In this study, several children with retrusive maxillas (chapter 8) had some form of nasal obstruction and choanal stenosis, which restricted the insertion of nasal airway and nasogastric tubes. In a single instance, nasal papillomas in a participant with Costello syndrome caused difficulty during this procedure.

Participants with microstomia, micrognathia and macroglossia had restricted access to the mouth. Visualization of the larynx was impaired and further compromised in children with enlarged tonsils and or adenoids. These difficulties were also encountered in those who had structural or functional abnormalities of the larynx, notably in the Rubinstein-Taybi, Hunter and Hurler syndromes.

17.2 Challenges accessing the larynx

Thickened aryepiglottic folds in the Costello syndrome decreased the diameter of the affected girl's airway, but after careful manipulation, the endotracheal tube was inserted without difficulty. Similar problems were encountered in two children with the Hunter syndrome in whom the tissues around the upper airway were congested. Kamin (2008) postulated that the deposition of glycosaminoglycans in these areas might contribute towards this phenomenon. During intubation, care was exercised to avoid traumatizing any oropharyngeal tumours that

may have been present in a child with Tuberous Sclerosis. Comparable measures were taken to circumvent injury to the stenosed trachea of a participant with Apert syndrome.

Challenges in accessing the larynx were also encountered during this study in children who had changes to the contour and structure of their ribs, short necks and immovable jaws. These abnormalities were mainly seen in participants with the Hunter and Hurler syndromes, but some were also present those with Prader-Willi and Bardet-Biedl syndromes.

Adequate flexion and extension of the lower cervical vertebra and the atlanto-occipital complex are important to provide visibility and access during endotracheal intubation. This is achieved by aligning of the axes of the trachea and oral cavity. In instances where there was a limited movement of the cervical spine such as in the Hunter syndrome, in children with kyphosis such as in the Rubinstein-Taybi syndrome and those with short necks, tracheal visibility and intubation became challenging. The genetic ID syndromes accompanied by short necks which were encountered in the study are listed in Table XVII.1. The references which are quoted pertain to contemporary publications in which the anaesthetic challenges of participants with short necks are documented.

Table XVII.1: Participants with short necks evaluated during the study

Syndrome	Reference
Costello	Katcher, Bothwell & Tobias, 2003; Williams, 2014; Akçıl, Dilmen & Tunalı, 2015
Hunter	Kamin 2008
Hurler	Gurumurthy et al., 2014
Kabuki	Atalay et al. 2014
Turner	Maranhão 2008

17.3 Challenges during airway management

One of the most critical requirements for successful dental management of a child with ID under GA is a clear and protected airway. Maintaining optimal oxygen levels during intubation is the foundation of successful airway management. Craniofacial anomalies in children with syndromic ID may influence the patency of the airways during GA procedures. The most common obstacle to airflow is a cleft lip and / or palate.

The participants examined during the survey with ID syndromes and accompanying clefts were discussed in chapter 8. All those referred for dental management with either or both conditions previously had surgical correction during infancy.

Fundamentally, clefts may not pose difficulties during airway management but they alter the anatomy of the palate by forming cavities. When these occur in the posterior areas of the palate, the tongue may occupy the transformed areas and obstruct the oropharynx (Sher, 1992). During the author's investigation, these changes were observed in the majority of children who had undergone cleft repairs. The level of airway maintenance in these instances depended on whether the clefts were bilateral or unilateral, as well as the integrity of the repair. Care was exercised in those with any form of airway obstruction including who had experienced postsurgical complications following the construction of a pharyngeal flap to correct a cleft palate or velopharyngeal insufficiency.

Maintaining the patency of the upper respiratory tract in participants with severe craniofacial anomalies, in particular, those with midface hypoplasia, also posed several callenges. When the affected children closed their mouths, their tongues filled the oral cavity and obstructed the upper airways. Similar problems were encountered in participants with macroglossia (chapter 8). Practical challenges such as the inability to position an anaesthetic mask and

excessive salivation during the GA procedures also increased the risk of upper airway obstruction.

There are numerous challenges that may be experienced before, during and after the dental treatment of children with ID under GA and in each instance, the author remained aware of these potential difficulties. The circumstances prior to the actual anaesthetic event such as the initial visit, clinical examination and careful documentation of the medical and dental histories contributed to the low morbidity rate experienced during the study.

17.4 Complications of general anaesthesia

17.4.1 Atlantoaxial subluxation.

A common concern in the dental anaesthetic management of children with genetic ID syndromes is atlantoaxial subluxation. This complication occurs as a consequence of instability of the atlanto-axial complex and is characterised by disproportionate movement at the joint between the atlas and axis of the cervical spine. The abnormal movement could be the result of either a skeletal abnormality or ligamentous laxity or a combination of both. Down syndrome is the most common form of genetic ID in which atlanto-axial instability may be a component. For this reason, care was exercised in children with Down syndrome who showed signs or had a history of atlanto-occipital instability during intubation. This management regime was crucial for the prevention of compression of the spinal cord.

17.4.2 Systemic complications

Children with genetic ID syndromes are susceptible to systemic complications during and after GA procedures. In those with structural abnormalities of the heart valves, the potential of developing infective endocarditis remained a concern. Likewise, the chronic ingestion of anticonvulsant drugs in children with seizures may potentially alter the metabolism of some anaesthetic drugs. Additional potential complications affecting the participants encountered

in this study are listed in Table XVII.2. The references which are quoted pertain to contemporary publications in which the anaesthetic complications of children with genetic ID syndromes are documented.

Table XVII.2: Potential systemic complications of GA in genetic ID syndromes

ORGAN	COMPLICATION	Syndrome	REFERENCES
Heart	Bradycardia	Angelman	Maguire 2009
		Down	Borland, Colligan & Brandom, 2004; Walia, Ruda & Tobias, 2016
	Tachycardia	Down	Beilin et al., 1988
	Arrythmias	Prader-Willi,Rubenstein Taybi	Lirk et al. 2004; Park et al. 2012
	Hypertension	Prader-Willi	Ananthanarayan et al. 1998
	Hyoptension	Down	Beilin et al. 1988
		Prader-Willi	Barbara, Hannon & Hartman, 2012
Lung	Bronchospasm	Apert	Patel et al. 2013
		Prader-Willi	Legrand & Tobias, 2006
	Respiratory infection	Down	Beilin et al. 1988
	Aspiration	Apert,	Basar et al. 2007;
		Bardet-Biedl	Baum & O'Flaherty 2007
		Down	Beilin et al. 1988
		Prader-Willi	Barbara, Hannon & Hartman, 2012
		Rubbenstein-Taybi	Karahan et al., 2016
	Postoperative pulmonary oedema	Hunter	Walker et al. 2003
		Prader-Wlli	Mantadakis et al., 2006
	Post operative atelectasis	Down	Beilin et al. 1988
	Desaturation	Bardet-Biedl	Baum & O'Flaherty 2007
		Down	Sinha et al., 2011
		Hunter	Kamin, 2008
		Prader-Willi	Mantadakis et al., 2006; Choi et al., 2012
	Hypoventilation	Prader – Willi	Barbara et al. 2012
	Apnea	Prader-Willi	Barbara et al. 2012
		Rubenstein-Taybi	Park, Park & Choi, 2012; Karahan et al., 2016
		Seckel	Grewal et al., 2014
	Wheezing	Apert	Elwood et al. 2001
Gastrointestinal Tract	Gastroesophageal reflux	Down	Beilin et al. 1988
		Rubenstein-Taybi	Park, Park & Choi, 2012
Central nervous system	Exacerbation of raised intracranial pressure	Apert	Kumar et al. 2014
	Hypotonia	Angelman	Butler et al. 2000
Kidney	Impaired function	Wolf-Hirschhorn	Kondo et al. 2013
Metabolic reactions	Malignant hyperthermia	Wolf-Hirschhorn	Haas, Young & Harper, 1992; Chen et al., 1994
		Prader-Willi	Mantadakis et al., 2006

References

1. Akçıl, E.F., Dilmen, Ö.K. & Tunalı, Y. 2015. Anaesthetic management in Costello syndrome. *Turkish Journal of Anaesthesiology and Reanimation*. 43(6):427–430. doi: 10.5152/TJAR.2015.93546.

2. Ananthanarayan, C., Sigal, M. & Godlewski, W. 1998. General anesthesia for the provision of dental treatment to adults with developmental disability. *Anesthesia Progress*. 45(1):12–17.

3. Atalay, Y.O., Kaya, C., Ustun, Y.B., Sahinoglu, A.H. 2014. Anesthesia management in a patient with Kabuki syndrome. *Medical Archives*. 68(5):359–4360. doi: 10.5455/medarh.2014.68.359-360.

4. Barbara, D.W., Hannon, J.D. & Hartman, W.R. 2012. Intraoperative adrenal insufficiency in a patient with Prader-Willi syndrome. *Journal of Clinical Medicine Research*. 4(5):346–348. doi: 10.4021/jocmr1039w.

5. Basar, H., Buyukkocak, U., Kaymak, C., Akpinar, S., Sert, O., Vargel, I. 2007. An intraoperative unexpected respiratory problem in a patient with Apert syndrome. *Minerva Anestesiologica*. 73(11):603–606.

6. Baum V & O'Flaherty J. 2007. *Anesthetic for Genetic, Metabolic and Dysmorphic Syndromes of Childhood*. 2nd ed. Philadelphia: Lippincott Williams and Wilkins.

7. Beilin, B., Kadari, A., Shapira, Y., Shulman, D., Davidson, J.T. 1988. Anaesthetic considerations in facial reconstruction for Down's syndrome. *Journal of the Royal Society of Medicine*. 81(1):23–26.

8. Borland, L.M., Colligan, J. & Brandom, B.W. 2004. Frequency of anesthesia-related complications in children with Down syndrome under general anesthesia for noncardiac procedures. *Paediatric Anaesthesia*. 14(9):733–738. doi: 10.1111/j.1460-9592.2004.01329. x.

9. Butler, M.G., Hayes, B.G., Hathaway, M.M., Begleiter, M.L. 2000. Specific genetic diseases at risk for sedation/anesthesia complications. *Anesthesia and Analgesia*. 91(4):837–855. doi: 10.1097/00000539-200010000-00014.

10. Chen, J.C., Jen, R.K., Hsu, Y.W., Ke, Y.B., Hwang, J.J., Wu, K.H., Wei, T.T. 1994. [4P- syndrome (Wolf-Hirschhorn syndrome) complicated with delay onset of malignant hyperthermia: a case report]. [Abstract]. *Acta Anaesthesiologica Sinica*. 32(4):275–278.

11. Choi, J.W., Kim, E.J., Min, B.W., Ban, J.S., Lee, S.G., Lee, J.H. 2012. Experience of severe desaturation during anesthetic induction period in an obese adult patient with Prader-Willi syndrome -A case report-. *Korean Journal of Anesthesiology*. 62(2):179–183. doi: 10.4097/kjae.2012.62.2.179.

12. Elwood, T., Sarathy, P. V, Geiduschek, J.M., Ulma, G.A., Karl, H.W. 2001. Respiratory complications during anaesthesia in Apert syndrome. *Paediatric Anaesthesia*. 11(6):701–703. doi: 10.1046/j.1460-9592.2001.00745. x.

13. Grewal, A., Sood, D., Bhatia, N., Garg, R., Shah, S., Kaur, H. 2014. Palatoplasty in a patient with Seckel syndrome: an anesthetic challenge. *Brazilian Journal of Anesthesiology.*64(3):216–218. doi: 10.1016/j.bjane.2013.08.005.

14. Gurumurthy, T., Shailaja, S., Kishan, S., Stephen, M. 2014. Management of an anticipated difficult airway in Hurler's syndrome. *Journal of Anaesthesiology, Clinical Pharmacology*. 30(4):558–561. doi: 10.4103/0970-9185.142862.

15. Haas, D.A., Young, E.R. & Harper, D.G. 1992. Malignant hyperthermia and the general dentist: current recommendations. *Journal of the Canadian Dental Association*. 58(1):28–33.

16. Kamin, W. 2008. Diagnosis and management of respiratory involvement in Hunter syndrome. *Acta Paediatrica*. 97(Suppl 457):57–60. doi: 10.1111/j.1651-2227.2008.00650. x.

17. Karahan, M.A., Sert, H., Ayhan, Z., Ayhan, B. 2016. Anaesthetic management of children with Rubinstein-Taybi syndrome. *Turkish Journal of Anaesthesiology and Reanimation*. 44(3):152–154. doi: 10.5152/TJAR.2016.76992.

18. Katcher, K., Bothwell, M. & Tobias, J.D. 2003. Anaesthetic implications of Costello syndrome. *Paediatric Anaesthesia*. 13(3):257–262.

19. Kondo, S., Okuyama, K., Ikemoto, K., Furuya, A., Matsukawa, T. 2013. General anesthesia for a boy with Wolf-Hirschhorn syndrome. *Japanese Journal of Anesthesiology*. [Abstract] 62(12):1466–1468.

20. Kumar, N., Arora, S., Bindra, A., Goyal, K. 2014. Anesthetic management of craniosynostosis repair in patient with Apert syndrome. *Saudi Journal of Anaesthesia*. 8(3):399–401. doi: 10.4103/1658-354X.136631.

21. Legrand, R. & Tobias, J.D. 2006. Anesthesia and Prader-Willi syndrome: preliminary experience with regional anesthesia. *Paediatric Anaesthesia*. 16(7):712–722. doi: 10.1111/j.1460-9592.2006.01968. x.

22. Lirk, P., Keller, C., Colvin, J., Rieder, J., Wulf, K. 2004. Anaesthetic management of the Prader-Willi syndrome. *European Journal of Anaesthesiology*. 21(10):831–833.

23. Maguire, M. 2009. Anaesthesia for an adult with Angelman syndrome. *Anaesthesia*. 64(11):1250–1253. doi: 10.1111/j.1365-2044.2009.06033. x.

24. Mantadakis, E., Spanaki, A.M., Geromarkaki, E., Vassilaki, E., Briassoulis, G. 2006. Near demise of a child with Prader-Willi syndrome during elective orchidopexy. *Paediatric Anaesthesia*. 16(7):790–793. doi: 10.1111/j.1460-9592.2006.01990. x.

25. Maranhão, M.V.M. 2008. Turner syndrome and anesthesia. *Revista Brasileira de Anestesiologia*. 58(1):84–89.

26. Park, C.H., Park, K.H. & Choi, B.Y. 2012. Management of anesthesia for Rubinstein-Taybi syndrome. *Korean Journal of Anesthesiology*. 63(6):571–572. doi: 10.4097/kjae.2012.63.6.571.

27. Patel, K., Chavan, D. & Sawant, P. 2013. Anesthesia management in a patient of Apert syndrome. *Anesthesia, Essays and Researches*. 7(1):133–135. doi: 10.4103/0259-1162.114021.

28. Sher, A.E. 1992. Mechanisms of airway obstruction in Robin sequence: implications for treatment. *The Cleft Palate-Craniofacial Journal*. 29(3):224–231. doi: 10.1597/1545-1569(1992)029<0224:MOAOIR>2.3.CO;2.

29. Sinha, R., Thangaswamy, C.R., Muthiah, T., Chandra, P., Subramaniam, R. 2011. Prolonged postoperative desaturation in a child with Down syndrome and atrial septal defect. *Indian Journal of Anaesthesia*. 55(6):608–610. doi: 10.4103/0019-5049.90619.

30. Walia, H., Ruda, J. & Tobias, J.D. 2016. Sevoflurane and bradycardia in infants with trisomy 21: a case report and review of the literature. *International Journal of Pediatric Otorhinolaryngology*. 80:5–7. doi: 10.1016/j.ijporl.2015.11.007.

31. Walker, R.W.M., Colovic, V., Robinson, D.N., Dearlove, O.R. 2003. Postobstructive pulmonary oedema during anaesthesia in children with mucopolysaccharidoses. *Paediatric Anaesthesia*. 13(5):441–447. doi: 10.1046/j.1460-9592.2003.00969. x.

32. Williams, C. 2014. Anesthetic Management of Costello Syndrome: a case report. *American Association of Nurse Anesthetists*. 82(2):108–113.

CHAPTER 18: CONSCIOUS SEDATION IN THE DENTAL MANAGEMENT OF CHILDREN WITH ID

Conscious sedation (CS) is “a technique in which the use of a drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation” (General Dental Council, 2005). During this process, the patients remain conscious, sustains their defensive reflexes, breathe consciously and independently and can respond to verbal instructions and physical stimulation.

The technique is an essential component of pain and anxiety management in dentistry, and it is often used instead of general anaesthesia (GA) thereby making it a widely sourced modality. Furthermore, CS induces a lighter form of sedation than GA. resulting in less respiratory and cardiac depression and involves less airway manipulation. It is cheaper as it requires less equipment and drugs and does not need an operating theatre.

General dentists offer CS in their private practices and it is also used with children attending State Dental clinics who are referred to the UWC Faculty of Dentistry, Tygerberg Hospital. This facility is equipped with specially trained personnel and specialized facilities that include consulting rooms furnished with monitors, positive pressure oxygen, high-speed suction apparatus and emergency kits. In the event of a crisis, an on-site emergency service is also available. Although CS was a preferred form of sedation for many participants in the study, long waiting lists precluded it from being used in most instances.

Several methods of administering CS are available to dental practitioners including inhalation, oral, intranasal, intravenous, rectal and intramuscular sedation techniques. At the UWC Faculty of Dentistry mainly intravenous and occasionally inhalation sedation are offered.

18.1 Patient selection

The selection of participants for dental management under CS during the study were in accordance with the guidelines promulgated by the South African Society of Anaesthesiologists (Reed et al., 2010). These were based on the child's age, general health, possible medical risks, the level of the child's anxiety, the extent of ID, the extent of dental treatment required, the cost and the availability of an anaesthesiologist. At the Faculty of Dentistry, UWC, the following specific criteria are followed when selecting children for CS:

- Have minimal inappropriate movement
- Weighs more than 15kg
- Above 3 years of age
- No or mild systemic problems
- Short dental procedures
- Mainly extractions

18.2 Preoperative procedures

The preoperative procedures were similar to those for children undergoing dental procedures under GA (chapter 15) and followed the protocol compiled by the UWC Faculty of Dentistry (addendum 6). In addition, the route and level of CS along with possible drug interactions were considered during this phase. Before undergoing CS, children were evaluated by a physician to establish whether they were medically suitable for the planned procedures to be undertaken.

Intravenous (IV) sedation was preferred for those older than 3 years, weighing 15kg or more and who were very anxious. This modality was contraindicated for individuals with concurrent liver disorders such as in the Down and Kabuki syndromes and Tuberous sclerosis

(chapter 13) and those with a history of sleep apnea. Children displaying mild anxiety, who could understand and respond to verbal commands and were over the age of 6 years received dental treatment with Nitrous Oxide sedation. However, to avoid possible complications, an alternative route of sedation was sought for individuals with a history of sleep apnea or of psychosis. Participants with enlarged tonsils and adenoids and those with structural problems of the breathing apparatus (chapter 13) were treated under general anaesthetic. All procedures were performed with the assisance of a trained anesthesiologist at the Faculty of Dentistry, UWC.

Informed consent was received from the childrens' parent or caregiver during the preoperative visit and a written instruction sheet detailing the requirements, and postoperative care was provided.

18.3 Risks of CS in managing children with ID

Although none of the children suffered significant complications after dental management, the author remained aware of these potential difficulties. Applegate et al. (2016) reported that approximately 70% of CS procedures are associated with undesirable cardiovascular and respiratory events. These are especially common in susceptible individuals such as patients with compromised immune systems. The authors also highlighted possible technical errors, such as defective recordings by ventilation monitoring devices, that may result in the inaccurate detection of hypoventilation during the CS process. For these reasons, this procedure was not deemed suitable for study participants who had respiratory disorders such as asthma, sleep apnea, enlarged adenoids or tonsils and laryngospasms. The genetic ID syndromes accompanied by sleep apnea which were encountered in the study are listed in

Table XVIII.1. The references which are quoted pertain to contemporary publications in which the anaesthetic challenges of children with sleep apnea are documented.

Table XVIII.1: Genetic ID syndromes associated with sleep apnea encountered in the survey

Syndrome	Reference
Coffin-Lowry	Imataka et al., 2016
Costello	Marca et al. 2006
Down	Subramaniam et al., 2016
Hunter	Tylki-Szymańska, 2014
Prader-Willi	Pavone et al., 2015
Rubenstein-Taybi	Blazquez et al., 2016
Sotos	Gomes-silva et al., 2006
Williams	Monfared and Messner 2006

Sedated children affected by apnea are at risk of developing an upper-airway obstruction which could result in hypoxemia and eventually desaturation (Ganzberg, 2016). In addition, they may also be hypersensitive to opioids. which may lead to respiratory depression (Brown, Laferrière & Moss, 2004).

Children with a combination of upper-airway obstruction and congenital heart disease have a high risk of developing pulmonary hypertension during dental treatment under CS (Yoshikawa et al., 2013).

18.4 Systemic considerations of CS in children with ID

Epileptic seizures during dental procedures are serious medical emergencies (chapter 10) and dental anxiety may trigger an unfavourable episode. For these reasons, CS was the preferred modality of sedation in healthy participants who had concurrent epilepsy. Due to its anti-convulsant properties, IV sedation with midazolam was preferred. However, other anticonvulsant drugs, routinely used by epileptic children, also depress the central nervous system and could interact with midazolam resulting in oversedation. For this reason, extra caution was warranted and the participants' vital signs were constantly monitored during all procedures.

Children with concurrent liver disorders were at risk of maintaining high levels of the drugs used for CS in their bloodstream and this may have resulted in prolonged recovery periods. Furthermore, those with concomitant anaemia were susceptible to the development of hypoxia during dental procedures under CS. This problem has occasionally been reported in genetic ID syndromes such as Bardet-Biedl syndrome (Asif et al., 2014); Seckel syndrome (Darrigo et al., 2014) and Down syndrome (Suzuki et al., 2016; Martínez-Macías et al., 2017).

Obesity is often associated with chronic extrinsic restrictive lung disease and together with cardiac and gastrointestinal problems can contribute to complications during CS (Baker & Yagiela, 2006).

Study participants who were visibly obese, including those with Biedl-Bardet (Forsythe et al., 2017) and Prader-Willi syndromes (Dykens, Roof & Hunt-Hawkins, 2017), had excessive adipose tissue in the area of the thorax and abdomen. This caused an increased pressure and hindered the movement of the diaphragm resulting in inefficient breathing that was clinically evident when they were in the supine position in the dental chair.

Vaughan and Wise (1976) postulated that these factors might lead to the closure of alveoli

and ultimately to atelectasis while lying down during sedation procedures. In addition, obese children require more oxygen to support normal tissue function. In order to maintain optimal function, these children breathe more rapidly, albeit shallowly. Drugs such as benzodiazepam routinely used in CS procedures depress the respiratory system and if not monitored correctly, may induce excessive accumulation of carbon dioxide and oxygen insufficiency during dental procedures performed in the supine position under CS.

The genetic ID syndromes accompanied by obesity which were encountered in the study were

18.5 General problems

Several challenges, which are not unique to managing children with ID, may manifest during CS procedures. These include the development of hypotension, problems with venepuncture, hiccups, nausea and vomiting, prolonged recovery, failed sedation, paradoxical effects, oversedation, undersedation, disinhibition and sexual fantasies. All events, irrespective of whether they were related to the dental procedure or the sedation process, were recorded in the participants' folders.

Comment

Although CS was considered a safe alternative to GA in managing anxiety and behaviour during dental treatment of the participants, several factors required consideration prior to, during and after dental procedures. During the author's investigation the risks, benefits and availability of particular sedation procedures were carefully considered when selecting children for the use of this approach.

References

1. Applegate, R.L., Lenart, J., Malkin, M., Meineke, M.N., Qoshlli, S., Neumann, M., Jacobson, J.P., Kruger, A., et al. 2016. Advanced monitoring is associated with fewer alarm events during planned moderate procedure-related sedation: a 2-part pilot trial. *Anesthesia and Analgesia*. 122(4):1070–1078. doi:10.1213/ane.0000000000001160.
2. Asif, M., Aziz, T., Altaf, S., Sattar, R.A. 2014. Laurence Moon Bardet Biedl syndrome with anaemia. *Journal of Ayub Medical College.*26(4):625–627.
3. Baker, S. & Yagiela, J.A. 2006. Obesity: a complicating factor for sedation in children. *Pediatric Dentistry*. 28(6):487–493.
4. Blazquez, E., Narvaez, D., Fernandez-Lopez, A., Garcia-Aparicio, L. 2016. Anesthetic management for thoracic surgery in Rubinstein-Taybi syndrome. *Revista Espanola de Anestesiologia Y Reanimacion*. 63(6):361–364. doi: 10.1016/j.redar.2016.02.004.
5. Brown, K.A., Laferrière, A. & Moss, I.R. 2004. Recurrent hypoxemia in young children with obstructive sleep apnea is associated with reduced opioid requirement for analgesia. *Anesthesiology*. 100(4):806–810.
6. Darrigo, L.G., Rodrigues, M.C., Pieroni, F., Stracieri, A.B.P.L., Moraes, D.A., Grecco, C.E.S., Dias, J.B.E., Sobral, A.C., et al. 2014. Successful outcome of allogeneic stem cell transplantation in Seckel syndrome. *Pediatric Transplantation*. 18(3):E93–E95. doi:10.1111/petr.12230.
7. Dykens, E.M., Roof, E. & Hunt-Hawkins, H. 2017. Cognitive and adaptive advantages of growth hormone treatment in children with Prader-Willi syndrome. *Journal of Child Psychology and Psychiatry*. 58(1):64–74. doi:10.1111/jcpp.12601.
8. Forsythe, E., Sparks, K., Best, S., Borrows, S., Hoskins, B., Sabir, A., Barrett, T., Williams, D., et al. 2017. Risk factors for severe renal disease in Bardet–Biedl syndrome. *Journal of the American Society of Nephrology*. 28(3):963–970. doi:10.1681/asn.2015091029.
9. Ganzberg, S. 2016. Obstructive sleep apnea and office-based surgery. *Anesthesia Progress*. 63(2):53–54. doi:10.2344/0003-3006-63.2.53.
10. General Dental Council. Standards for Dental Professionals.2005. London: The General. Dental Council.
11. Gomes-Silva, J.M., Ruviere, D.B., Segatto, R.A., de Queiroz, A.M., de Freitas, A.C. 2006. Sotos syndrome: a case report. Special Care in Dentistry. 26(6):257–262.
12. Imataka, G., Nakajima, I., Goto, K., Konno, W., Hirabayashi, H., Arisaka, O. 2016. Drop episodes improved after tracheotomy: a case of Coffin-Lowry syndrome associated with obstructive sleep apnea syndrome. *European Review for Medical and Pharmacological Sciences*. 20(3):498–501.
13. Marca, G. Della, Vasta, I., Scarano, E., Rigante, M., De Feo, E., Mariotti, P., Rubino, M., Vollono, C., et al. 2006. Obstructive sleep apnea in Costello syndrome. *American Journal of Medical Genetics Part A*. 140(3):257–262. doi:10.1002/ajmg.a.31076.

14. Martínez-Macías, F.J., Bobadilla-Morales, L., González-Cruz, J., Quiles-Corona, M., Corona-Rivera, A., Peña-Padilla, C., Orozco-Vela, M., Silva-Cruz, R., et al. 2017. Descriptive study of the complete blood count in newborn infants with Down syndrome. *American Journal of Medical Genetics Part A*. 173(4):897-904. doi: 10.1002/ajmg.a.38097.
15. Monfared, A. & Messner, A. 2006. Death following tonsillectomy in a child with Williams syndrome. *International Journal of Pediatric Otorhinolaryngology*. 70(6):1133–1135. doi: 10.1016/j.ijporl.2005.11.009.
16. Pavone, M., Caldarelli, V., Khirani, S., Colella, M., Ramirez, A., Aubertin, G., Crinò, A., Brioude, F., et al.2015. S. Disordered breathing in patients with Prader-Willi. syndrome: a. multicenter study. *Pediatric Pulmonology*. 50(12):1354–1359. doi:10.1002/ppul.23177.
17. Reed, A., Thomas, J., Roelofse, J., Gray, R. 2010. Guidelines for the safe use of procedural sedation and analgesia for diagnostic and therapeutic procedures in children. *South African Journal of Anesthesia and Analgesia*. 16(5):S1–S37.
18. Subramaniam, D.R., Mylavarapu, G., McConnell, K., Fleck, R.J., Shott, S.R., Amin, R.S., Gutmark, E.J. 2016. Upper airway elasticity estimation in pediatric Down Syndrome sleep apnea patients using collapsible tube theory. *Annals of Biomedical Engineering*. 44(5):1538–1552. doi:10.1007/s10439-015-1430-4.
19. Suzuki, K., Muramatsu, H., Okuno, Y., Narita, A., Hama, A., Takahashi, Y., Yoshida, M., Horikoshi, Y., et al. 2016. Immunosuppressive therapy for patients with Down syndrome and idiopathic aplastic anemia. *International Journal of Hematology*. 104(1):130–133. doi:10.1007/s12185-016-1997-z.
20. Tylki-Szymańska, A. 2014. Mucopolysaccharidosis type II, Hunter's syndrome. *Pediatric Endocrinology Reviews*. 12:107–113. doi:10.1001/archderm.102.5.578.
21. Vaughan, R.W. & Wise, L. 1976. Intraoperative Arterial oxygenation in obese patients. *Annals of Surgery*. 184(1):35–42.
22. Yoshikawa, F., Tamaki, Y., Okumura, H., Miwa, Z., Ishikawa, M., Shimoyama, K., Nakamura, Z., Kunimori, H., et al. 2013. Risk factors with intravenous sedation for patients with disabilities. *Anesthesia Progress*. 60(4):153–161. doi:10.2344/0003-3006-60.4.153.

CHAPTER 19: BARRIERS TO ORAL HEALTH CARE IN CHILDREN WITH ID

Introduction

South Africa, being multicultural, multilingual and mulitsocial with varying levels of income, education and perceptions, presents unique challenges for a unified approach to oral health services.

Reasons for non-attendance of dental clinics vary across categories of individuals and are intimately interrelated. While the international literature mainly focuses on the obstacles faced by minority groups in accessing oral health care, the majority of South Africans experience similar adversity. These constraints mostly occur because of factors inherent in the country's historical and political background.

The challenges that children with ID face are complex and often interconnected. These affect not only the oral health but also their psychological well-being. This chapter describes the barriers children with ID face when attempting to access oral health care. The content is based on informal conversations held between the author and the children's parents and or caregivers.

19.1 Financial barriers

19.1.1 Unemployment

Unemployment and poverty are intimately related, and both significantly influence the quality of life and access to basic requirements such as food, clean drinking water and sanitation, educational facilities, health care and safety. Poverty also results in social ills such as drug abuse, violence and an increase in communicable diseases such as tuberculosis and HIV as well as mental illnesses such as depression.

Unemployment has both direct and indirect implications for access to and utilization of oral health care facilities. The inability to pay for oral health or transportation to dental services is a primary consequence of unemployment.

South Africa has a chronically high unemployment rate recently amounting to 26% (Statistics South Africa 2016). The context in which this study was conducted was often a reflection of the consequences of unemployment and poverty and families were often in need of food and other necessities. Apart from high travelling costs, the cost of children's general health care needs and treatment for their disability such as medicines and travelling for rehabilitation therapy added to some parent's financial constraints. In addition, many of the children were cared for by single parents or grandparents and their families relied on minimal funding from the state for basic food and security.

19.1.2 Medical Aid (insurance)

A minority of South Africans are covered by private medical aid (insurance) and most of the population either pay dental services out-of-pocket or rely on the state to pay or subsidise dental fees. Furthermore, many medical aid providers limit the amount of money allocated for dentistry while some medical services may not accept certain medical aid schemes. The majority of children involved in this investigation relied on the state-subsidized health services and only a few parents were in a position to request a referral to a private dental practitioner for further dental management.

The enormous cost of dental procedures for both medical aid beneficiaries and state-dependant individuals, especially those requiring specialized treatment such as orthodontic intervention, could in part, account for the low rates of dental visits and high prevalence of oral disease observed during this study.

19.2 Non-utilization of oral health care services

The low-utilization of oral health services is not unique to South Africa. International studies among HIV-positive individuals (Pereyra et al., 2011), children (George et al., 2013), persons living in rural populations (Mariño et al., 2014) and pregnant women (Silveira et al., 2016) reported similar trends.

In a recent unpublished survey conducted by students Madhoo et al (2013) and other students at the UWC Dental Faculty, it emerged that taking time away from work was the primary reason for patients failing to utilize dental services after their initial visit. The students' findings were echoed by some of the employed parents of children involved in the current study. Long waiting times for a visit often translated into more time away from work for these parents, which resulted in a further loss of income. Additionally, some parents mentioned that the long queues and extended periods of treatment also inhibited them from returning with their children to the dental clinic.

19.3 Education

Although there is an association between education and unemployment, the level of an individual's education does not necessarily affect their income status but does play a role in behaviour, personal choices and perceptions of oral health care. These characteristics are also influenced by their social and demographic environment. Conversely, a high level of education does not always translate into adequate oral health literacy.

19.3.1 Parents' and Caregivers' oral health literacy and perceptions

During casual conversations with parents and caregivers of the children involved in the study, a few mentioned that they were unaware of oral health problems experienced by their children and indicated that they would seek treatment if the children complained of pain or "bleeding gums". Many parents were also unaware of the significance of the primary teeth and were not familiar with preventative strategies such as scaling and polishing and fissure sealants. These deficiencies may have influenced the high prevalence of dental needs in the children involved in the author's investigation and echo findings reported in the literature among children in the general population (Miller et al., 2010; Khodadadi et al., 2016).

19.3.2 Oral health literacy among general medical staff

The study participants were referred directly or indirectly from the Medical Genetics Unit, University of Cape. The genetics team included medical geneticists, genetic councillors and nurses as well as permanent staff at the individual schools. These medically trained individuals were able to detect potential and pre-existing dental problems of children with ID. This situation highlights the important role that health professionals play in the dental screening and referral process of children who do not have direct access to oral care facilities.

19.4 Dental services available to children with ID

The children with dental problems and ID were had access to the dental services at three sites provided by the Faculty of Dentistry, UWC in the Western Cape. However, the parents and caregivers who sought treatment for their children with ID prior to the investigation often mentioned that they had limited opportunities to dental services at state facilities. The reasons for this included long waiting lists for preventative and emergency dental treatment

and not knowing the location of the facilities. Moreover, in some centres there was perceived reluctance and limited availability of the dentist to provide care for their children.

19.5 Violence

19.5.1 Violence against children

South Africa has one of the highest crime rates in the world of which contact crime constituted approximately 35% between 2015 and 2016. "Contact crime refers to those crimes in which the victims themselves are the targets of violence or property is targeted, and the victims in the vicinity during the commission of the crime are subjected to threats of violence or the use of such violence" (SAPS, 2016). In the USA, the most common violent acts that children with ID and their caregivers are exposed to are assault and sexual offences. The parents of children with ID experience high levels of stress especially those of children with severe forms of ID and those with extreme behavioural problems. These children are at a higher risk of experiencing physical violence (American Academy of Pediatrics 2001).

There is a higher frequency of sexual violence among children and adolescents with ID than among those in the general population, and their perpetrators are often either family members, caregiver or persons known to the family. In addition, children with ID are exposed to more forms of sexual abuse than children without ID and seldom report incidences of sexual assault (Soylu et al., 2013).

During the investigation, parents and caregivers often spoke about how the emotional, physical and financial support needed by their children resulted in extreme personal anxiety. While some parents had a stable family support structure to assist in the day to day care of their children, others stated that the only time they had relief from their responsibilities was when their children attended school. Occasionally, foster parents would express concern

about their ability to adequately care for these children's specific medical and psychological needs.

In South Africa, medical practitioners and dentists are obligated to report suspected cases of abuse and neglect to the Director-General or an officer of the Department of Social Development. The author considered herself adequately trained in the disciplines of Oral Medicine and Oral Pathology to detect evidence of sexual abuse during the study. The clinical signs of sexual abuse included oral and perioral features of sexually transmitted diseases, traumatic lesions in the oral cavity and the presence of bite marks. Similarly, signs of physical abuse included injuries to the head, face and neck, traumatic lesions to the teeth, lacerations of the oral and perioral soft tissues and fractures of the bones of the face and jaws.

19.5.2 Interpersonal violence amongst parents

The parents of abused children would often refrain from seeking either medical or dental treatment. In some instances, the nursing staff at the SE Facilities or visiting physicians detected subtle signs of abuse during routine examinations. On rare occasions when suspicious changes were observed in children's facial areas, the author questioned parents or caregivers as to the cause of the lesions but could seldom elicit a satisfactory response.

Intimate partner violence (IPV) directed toward the mother or caregiver of children with ID may have directly or indirectly influenced the frequency of their children's attendance at dental facilities. Women experiencing IPV avoid accessing health care services for reasons such as shame and fear (Lucea et al., 2013; Prosman, Lo Fo Wong & Lagro-Janssen, 2014). These emotional states may prevent them from seeking the necessary assistance for the children lest they themselves or their children are questioned about the circumstances surrounding their trauma.

Concluding comments:

Apart from their ID, physical and general health challenges, the participants in this study faced several additional challenges. Their experiences within their home or institutional environments and well as in their broader communities may have contributed to their deficient oral health. The high rate of unemployment, violence, drug abuse, poverty, lack of access to oral health care facilities in South Africa are some of the socioeconomic challenges faced by children with ID. Their plight is much greater than that of children without ID and with the current financial and political trends in the country, these problems may not improve in the short-term.

References

1. American Academy of Pediatrics. 2001. Committee on Child Abuse and Neglect and Committee on Children with Disabilities. Assessment of maltreatment of children with disabilities. *Pediatrics*. 108(2):508–512
2. George, A., Johnson, M., Blinkhorn, A., Ajwani, S., Ellis, S., Bhole, S. 2013. Views of pregnant women in South Western Sydney towards dental care and an oral-health program initiated by midwives. *Health Promotion Journal of Australia*. 24(3):178. doi: 10.1071/HE13040.
3. Khodadadi, E., Niknahad, A., Sistani, M.M.N., Motallebnejad, M. 2016. Parents' oral health literacy and its impact on their children's dental health status. *Electronic Physician*. 8(12):3421–3425. doi: 10.19082/3421.
4. Lucea, M.B., Stockman, J.K., Mana-Ay, M., Bertrand, D., Callwood, G.B., Coverston, C.R., Campbell, D.W., Campbell, J.C. 2013. Factors influencing resource use by African American and African Caribbean women disclosing intimate partner violence. *Journal of Interpersonal Violence*. 28(8):1617–1641. doi: 10.1177/0886260512468326.
5. Madhoo, S., Kandombo, C., Majozi, N. & Louw, N.E. 2013.Barriers to oral health care in Cape Town. [Unpublished]
6. Mariño, R.J., Khan, A.R., Tham, R., Khew, C.W., Stevenson, C. 2014. Pattern and factors associated with utilization of dental services among older adults in rural Victoria. *Australian Dental Journal*. 59(4):504–510. doi: 10.1111/adj.12216.
7. Miller, E., Lee, J.Y., DeWalt, D.A., Vann, W.F. 2010. Impact of caregiver literacy on children's oral health outcomes. *Pediatrics*. 126(1):107–114. doi: 10.1542/peds.2009-2887.
8. Pereyra, M., Metsch, L.R., Tomar, S., Valverde, E., Jeanty, Y., Messinger, S., Boza, H. 2011. Utilization of dental care services among low-income HIV-positive persons receiving primary care in South Florida. *AIDS Care*.23(1):98–106.doi: 10.1080/09540121.2010.498861.
9. Prosman, G.J., Lo Fo Wong, S.H., Lagro-Janssen, A.L.M. 2014. Why abused women do not seek professional help: a qualitative study. *Scandinavian Journal of Caring Sciences*. 28(1):3–11. doi: 10.1111/scs.12025.
10. SAPS. 2016. Crime situation in South Africa April 2015 -March 2016. Available: http://www.saps.gov.za/services/final-crime-stats-release-02september2016.pdf.
11. Silveira, M.L., Whitcomb, B.W., Pekow, P., Carbone, E.T., Chasan-Taber, L. 2016. Anxiety, depression, and oral health among US pregnant women: behavioral risk factor surveillance system. *Journal of Public Health Dentistry*. 76(1):56–64.doi: 10.1111/jphd.12112.
12. Soylu, N., Alpaslan, A.H., Ayaz, M., Esenyel, S., Oruç, M. 2013. Psychiatric disorders and characteristics of abuse in sexually abused children and adolescents with and without intellectual disabilities. *Research in Developmental Disabilities*. 34(12):4334–4342. doi: 10.1016/j.ridd.2013.09.010.
13. Statistics South Africa. 2016. *Work and Labour Force: South Africa*. Available: http://www.statssa.gov.za/?cat=31 [2017, March 08].

CHAPTER 20: CONCLUSION

Introduction

This chapter presents the concluding remarks and outlines advances in dental practises which are based on the findings of the study.

20.1 Contribution to knowledge.

To the best of the author's understanding, only a limited amount of research has been previously conducted in the investigation of the dental implications of ID in South Africa and in particular, Cape Town. This is the first study that was conducted in South Africa that investigated the prevalence of both avoidable and developmental oral disorders in children with ID in South Africa.

The project produced substantial information that provides insight to the oral health status of children with ID in Cape Town. It exceeded simple documentation of the prevalence of the oral disease and comprehensively addressed possible genetic causes of each dental problem. The interrelatedness of individual oral conditions and the management implications of each disorder were addressed. Furthermore, the obstacles to provide dental care to this group of children both in the dental office and the operating theatre were documented. It identified new insights associated with the dental and management implications of children with ID and integrated these perceptions with previous concepts and experiences from the literature.

Although this study concentrates on one area in Cape Town, the majority of challenges are relevant to any under-resourced location.

20.2 Recommendations

Dental training

- Human genetics should be formalized in the dental curriculum.
- Undergraduate and postgraduate dental students should have more exposure to the treatment of children with ID and genetic ID syndromes.
- Oral health education programmes specifically targeting the parents and caregivers of children with ID should be arranged.
- Dental professionals should promote universal primary dental services for persons with ID.
- Oral health professionals should familiarize themselves with the general principles of genetic counselling.

Oral Health education- parents and caregivers of children with ID

- **Educating the parent about**
    - Bottle feeding and weening.
    - Diet.
    - Overseeing daily oral health care routines.
    - Provision of psychological support for parents\caregivers\teachers.
- **Children with ID should be provided with**
    - Regular instructions on how to brush their teeth and why it is important. These can be in the form of technological aids, role playing and video games.
    - Access to basic oral hygiene tools such as toothpaste, tooth brushes and floss.
    - Access to specialized oral health facilities, not necessary wait in long queues or on waiting lists.

- **Government and nongovernmental organisations**
    - Highlight the importance of oral health in the medical curriculum and among non-dental medical professionals.
    - Promote and fund genetic testing for children with ID.
    - Implement surveillance and monitoring systems for oral diseases among children with ID to develop and refine oral health policies
    - Implement the Oral Health Care Policies for persons with disabilities.
    - Provide funding for additional and mobile oral health care facilities.
    - Support and promote specialized dental training for persons with ID and other disabilities.

Addendum 1

References

1. AAIDD. 2013. *Definition of Intellectual Disability*. Available: http://aaidd.org/intellectual-disability/definition#.Vo-U6vl96zc.
2. Abanto, J., Paiva, S.M., Raggio, D.P., Celiberti, P., Aldrigui, J.M., Bönecker, M. 2012. The impact of dental caries and trauma in children on family quality of life. *Community Dentistry and Oral Epidemiology*. 40(4):323–331. doi: 10.1111/j.1600-0528.2012.00672. x.
3. Abdalla E, Mostowska A, Jagodziński P, Dwidar K, I.S. 2014. A novel *WNT10A* mutation causes non-syndromic hypodontia in an Egyptian family. *Archives of Oral Biology*. 59(7):722–728. doi: 10.1016/j.archoralbio.2014.04.004.
4. Abdel-Salam, G.M., Afifi, H.H., Eid, M.M., El-Badry, T.H.,Kholoussi, N. 2011. Ectodermal abnormalities in patients with Kabuki syndrome. *Pediatric Dermatology*. 28(5):507–511. doi:10.1111/j.1525-1470.2011.01495. x.
5. Abe, K., Ooshima, T., Lily, T.S., Yasufuku, Y., Sobue, S. 1988. Structural deformities of deciduous teeth in patients with hypophosphatemic vitamin D-resistant rickets. *Oral Surgery, Oral Medicine, and Oral Pathology*. 65(2):191–198.
6. Abijeth, B., Kumar, S. & Durgha, K. 2015. Dental anomalies and oral hygiene status in mentally retarded children. *Asian Journal of Pharmaceutical and Clinical Research*. 8(5):195–198.
7. Adnams, C.M. 2010. Perspectives of intellectual disability in South Africa: epidemiology, policy, services for children and adults. *Current Opinion in Psychiatry*. 23(5):436–440. doi: 10.1097/yco.0b013e32833cfc2d.
8. Agochukwu, N.B., Solomon, B.D. & Muenke, M. 2014. Hearing loss in syndromic craniosynostoses: introduction and consideration of mechanisms. *American Journal of Audiology*. 23(2):135–141. doi:10.1044/2014_aja-13-0036.
9. Agrawal, M., Maitin, N., Rastogi, K.,Bhushan, R. 2013. Seeing the unseen: diagnosing acromegaly in a dental setup. *BMJ Case Reports*. 2013. doi: 10.1136/bcr-2013-200266.
10. Ahmed, M., Ura, K. & Streit, A. 2015. Auditory hair cell defects as potential cause for sensorineural deafness in Wolf-Hirschhorn syndrome. *Disease Models & Mechanisms*. 8(9):1027–1035. doi:10.1242/dmm.019547.
11. Ahrens-Nicklas, R.C., Reichert, S.L., Zackai, E.H.,Kaplan, P.B. 2015. Atypical Williams syndrome in an infant with complete atrioventricular canal defect. *American Journal of Medical Genetics. Part A*. 167(12):3108–3112. doi:10.1002/ajmg.a.37288.
12. Aida, J., Kondo, K., Yamamoto, T., Hirai, H., Nakade, M., Osaka, K., Sheiham, A., Tsakos, G., Watt, R.G.2011. Oral health and cancer, cardiovascular, and respiratory mortality of Japanese. *Journal of Dental Research*. 90(9): 1129–1135

13. Akar, H., Akar, G.C., Carrero, J.J., Stenvinkel, P., Lindholm, B., 2011. Systemic consequences of poor oral health in chronic kidney disease patients. *Clinical Journal of the American Society of Nephrology.* 6(1): 218–226.
14. Akcalı, A., Lang, N.P.2018. Dental calculus: the calcified biofilm and its role in disease development. *Periodontology 2000.* 76(1): 109–115. doi.10.1111/prd.12151
15. Akçıl, E.F., Dilmen, Ö.K. & Tunalı, Y. 2015. Anaesthetic management in Costello syndrome. *Turkish Journal of Anaesthesiology and Reanimation*. 43(6):427–430. doi: 10.5152/TJAR.2015.93546.
16. Alaki, S. & Bakry, N.2012. Dental Pain in Children with Intellectual Disabilities: Caregivers' Perspective. *International Journal of Dentistry*, 2012:1-7. doi: 10.1155/2012/701608.
17. Al-Ani, A., Antoun, J., Thomson, W., Merriman, T. & Farella, M. 2017. Hypodontia: An update on its etiology, classification, and clinical management. *BioMed Research International*, 2017:1-9.
18. Albandar, J.M., Buischi, Y.A., Axelsson, P. 1995. Caries lesions and dental restorations as predisposing factors in the progression of periodontal diseases in adolescents. A 3-year longitudinal study. *Journal of Periodontology.* 66(4): 249–254. doi.10.1902/jop.1995.66.4.249
19. Albert, D. A., Ward, A., Allweiss, P., Graves, D.T., Knowler, W.C., Kunzel, C., Leibel, R.L., Novak, K.F., et al. 2012. Diabetes and oral disease: implications for health professionals. *Annals of the New York Academy of Sciences*. 1255:1–15. doi:10.1111/j.1749-6632.2011.06460. x.
20. Aliaga, M. & Gunderson, B. 2000. Interactive Statistics. *The Statistics Teacher Network*. 53:1–7. doi: 10.2307/40074316.
21. Alió, J., Lorenzo, J., Iglesias, M.C., Manso, F.J., Ramírez, E.M. 2011. Longitudinal maxillary growth in Down syndrome patients. *Angle Orthodontist*. 81(2):253–259. doi: 10.2319/040510-189.1.
22. Alkhzouz, C., Lazea, C., Bucerzan, S., Nascu, I., Kiss, E., Denes, C.L.,Grigorescu-Sido, P. 2016. Clinical and genetic characteristics of Romanian patients mucopolysaccharidosis type II. *JIMD Reports*. (29):1–7. doi:10.1007/8904_2016_535.
23. Allanson, J.E. & Hennekam, R.C. 1997. Rubinstein-Taybi syndrome: objective evaluation of craniofacial structure. *American Journal of Medical Genetics*. 71(4):414–419.
24. Altun, C., Guven, G., Akgun, O.M., Akkurt, M.D., Basak, F., Akbulut, E. 2010. Oral health status of disabled individuals attending special schools. *European Journal of Dentistry*. 4:361–366.
25. American Academy Of Pediatric Dentistry. 2011. Guideline on Behavior Guidance for the Pediatric Dental Patient: Reference Manual. *American Academy of Pediatric Dentistry*. 36(6):179–191.
26. American Academy of Pediatrics. 2001. Committee on Child Abuse and Neglect and Committee on Children with Disabilities. Assessment of maltreatment of children with disabilities. *Pediatrics*. 108(2):508–512
27. American Diabetes Association. 2009. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 32.(Suppl. 1): S62-S67. doi:10.2337/dc09-s062.

28. American Heart Association. 2016. *Antibiotic Prophylaxis Prior to Dental Procedures*. Available: http://www.ada.org/en/member-center/oral-health-topics/antibiotic-prophylaxis.
29. Aminabadi, N.A., Ganji, A.T., Vafaei, A., Pourkazemi, M. & Oskouei, S.G. 2009. Oculodentodigital dysplasia: disease spectrum in an eight-year-old boy, his parents and a sibling. *Journal of Clinical Pediatric Dentistry*. 33(4):337–341.
30. Aminabadi, N.A., Pourkazemi, M., Oskouei, S.G. & Jamali, Z. 2010. Dental management of Oculodentodigital dysplasia: a case report. *Journal of Oral Science*. 52(2):337–342. doi:jst.jstage/josnusd/52.337.
31. Ananthanarayan, C., Sigal, M. & Godlewski, W. 1998. General anesthesia for the provision of dental treatment to adults with developmental disability. *Anesthesia Progress*. 45(1):12–17.
32. Anders, P.L. & Davis, E.L. 2010. Oral health of patients with intellectual disabilities: a systematic review. *Special Care in Dentistry*. 30(3):110–117. doi: 10.1111/j.1754-4505.2010.00136. x.
33. Andersson, E.M., Axelsson, S., Gjølstad, L. F. & Storhaug, K. 2013. Taurodontism: a minor diagnostic criterion in Laurence-Moon/Bardet-Biedl syndromes. *Acta Odontologica Scandinavica*. 71(6):1671–1674. doi:10.3109/00016357.2013.794389.
34. Anichini, C., Lotti, F., Pietrini, A., Lo Rizzo, C., Longini, M., Proietti, F., Felici, C.,Buonocore, G. 2013. Antioxidant effects of potassium ascorbate with ribose in Costello syndrome. *Anticancer Research*. 33(2):691–695.
35. Applegate, R.L., Lenart, J., Malkin, M., Meineke, M.N., Qoshlli, S., Neumann, M., Jacobson, J.P., Kruger, A., et al. 2016. Advanced monitoring is associated with fewer alarm events during planned moderate procedure-related sedation: a 2-part pilot trial. *Anesthesia and Analgesia*. 122(4):1070–1078. doi:10.1213/ane.0000000000001160.
36. Aragon, C.E. & Burneo, J.G. 2007. Understanding the patient with epilepsy and seizures in the dental practice. *Journal of the Canadian Dental Association*. 73(1):71–76.
37. Aroon, S. 1989. Social and psychological improvement of two handicapped patients by oral rehabilitation. *Journal of the Dental Association of Thailand*. 39(6):209–218.
38. Arora, S., Rattan, V. & Ghai, B. 2012. Anesthetic management of a child with Seckel syndrome for multiple extractions and restoration of teeth. *Journal of Anaesthesiology Clinical Pharmacology*. 28(3): 398-399.doi:10.4103/0970-9185.98361.
39. Asif, M., Aziz, T., Altaf, S., Sattar, R.A. 2014. Laurence Moon Bardet Biedl syndrome with anaemia. *Journal of Ayub Medical College*.26(4):625–627.
40. Atalay, Y.O., Kaya, C., Ustun, Y.B., Sahinoglu, A.H. 2014. Anesthesia management in a patient with Kabuki syndrome. *Medical Archives*. 68(5):359–360. DOI: 10.5455/medarh.2014.68.359-360.
41. Atar, M., Lee, W. & O'Donnell, D. 2006. Kabuki syndrome: Oral and general features seen in a 2-year-old Chinese boy. *International Journal of Paediatric Dentistry*. 16(3):222–226. doi: 10.1111/j.1365-263X.2006.00699. x.

42. Austin, D.E., Gunn, A.J. & Jefferies, C.A. 2015. Severe short stature and Wolf-Hirschhorn syndrome: response to growth hormone in two cases without growth hormone deficiency. *Oxford Medical Case Reports*. 2015(2):211–214. doi:10.1093/omcr/omv008.
43. Axelsson, S., Bjornland, T., Kjaer, I., Heiberg, A., Storhaug, K. 2003. Dental characteristics in Williams syndrome: a clinical and radiographic evaluation. *Acta Odontologica Scandinavica*. 61(3):129–136.
44. Aytekin, S. & Alyamac, G. 2013. Two new cases with Costello syndrome. *Dermatology Online Journal*. 19(8):19267.
45. Bai, H., Agula, H., Wu, Q., Zhou, W., Sun, Y., Qi, Y., Latu, S., Chen, Y., et al. 2010. A novel *DSPP* mutation causes dentinogenesis imperfecta type II in a large mongolian family. *BMC Medical Genetics*. 11:23. doi:10.1186/1471-2350-11-23.
46. Bajracharya, P., Bhatnagar, S. & Pauliks, L.B. 2011. Mitral valve diseases in Williams syndrome-case report and review of the literature. *Echocardiography*. 28(8):E156-159. doi:10.1111/j.1540-8175.2011.01423. x.
47. Baker, S. & Yagiela, J.A. 2006. Obesity: a complicating factor for sedation in children. *Pediatric Dentistry*. 28(6):487–493.
48. Bamjee,Y., Chikte, U. & Cleaton-Jones, P. 1999. Assessment of periodontal status and treatment needs of a disabled population using the CPITN. *South African Dental Journal*. 54(9):413–417.
49. Banks, L.M., Zuurmond, M., Ferrand, R., Kuper, H. 2015. The relationship between HIV and prevalence of disabilities in Sub-saharan Africa: systematic review. *Tropical Medicine and International Health*. 20(4):411–429. doi:10.1111/tmi.12449.
50. Barbara, D.W., Hannon, J.D. & Hartman, W.R. 2012. Intraoperative adrenal insufficiency in a patient with Prader-Willi syndrome. *Journal of Clinical Medicine Research*. 4(5):346–348. doi: 10.4021/jocmr1039w.
51. Barozzi,S., Di Berardino,F., Atzeri, F., Filipponi, E., Cerutti, M., Selicorni, A. C. 2009. Audiological and vestibular findings in the Kabuki syndrome. *American Journal of Medical Genetics, Part A.* 149(2):171–176. doi:10.1002/ajmg.a.32610.
52. Basar, H., Buyukkocak, U., Kaymak, C., Akpinar, S., Sert, O., Vargel, I. 2007. An intraoperative unexpected respiratory problem in a patient with Apert syndrome. *Minerva Anestesiologica*. 73(11):603–606.
53. Battaglia, A., Filippi, T. & Carey, J.C. 2008. Update on the clinical features and natural history of Wolf-Hirschhorn (4p-) syndrome: experience with 87 patients and recommendations for routine health supervision. *American Journal of Medical Genetics. Part C.* 148(4):246–51. doi:10.1002/ajmg.c.30187.
54. Baum V & O'Flaherty J. 2007. *Anesthetic for Genetic, Metabolic and Dysmorphic Syndromes of Childhood*. 2nd ed. Philadelphia: Lippincott Williams and Wilkins.
55. Bay, M & Lipkin, P.2011.Intellectual Disability: historical note and nomenclature. Available at: http://www.medmerits.com/index.php/article/intellectual_disability/P1. [Accessed: 2016-01-19]

56. Bayram, M., Yildirim, M. & Seymen, F. 2015. Clinical and oral findings of a patient with Simpson-Golabi-Behmel syndrome. *European Archives of Paediatric Dentistry.* 16(1):63–66. doi: 10.1007/s40368-014-0141-0.
57. Bazopoulou-Kyrkanidou, E. & Papagiannoulis, L. 1992. Prader-Willi syndrome: report of a case with special emphasis on oral problems. *Journal of Clinical Pediatric Dentistry*. 17(1):37–40.
58. Beadle-Brown, J., Mansell, J. &, Komza, A. 2007. Deinstitutionalization in intellectual disabilities. *Current Opinions in Psychiatry*. 20(5):437–442. doi:10.1097/YCO.0b013e32827b14ab.
59. Beales, P.L., Warner, A.M., Hitman, G.A., Thakker, R., Flinter, F.A. 1997. Bardet-Biedl syndrome: a molecular and phenotypic study of 18 families. *Journal of Medical Genetics*. 34(2):92–98.
60. Beales, P.L., Elcioglu, N., Woolf, A.S., Parker, D., Flinter, F.A. 1999. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *Journal of Medical Genetics*. 36(6):437–446
61. Beena, J.P. 2011. Prevalence of dental caries and its correlation with the immunologic profile in HIV-infected children on antiretroviral therapy. *European Journal of Paediatric Dentistry*. 12(2):87–90.
62. Beets, L., Rodríguez-Fonseca, C. & Hennekam, R.C. 2014. Growth charts for individuals with Rubinstein-Taybi syndrome. *American Journal of Medical Genetics. Part A*. 164(9):2300–2309. doi:10.1002/ajmg.a.36654.
63. Beilin, B., Kadari, A., Shapira, Y., Shulman, D.,Davidson, J.T. 1988. Anaesthetic considerations in facial reconstruction for Down's syndrome. *Journal of the Royal Society of Medicine*. 81(1):23–26.
64. Benzian, H., Monse, B., Heinrich-Weltzien, R., Hobdell, M., Mulder, J.,van Palenstein Helderman, W. 2011. Untreated severe dental decay: a neglected determinant of low body mass index in 12-year-old Filipino children. *BMC Public Health*. 11(1):558. doi: 10.1186/1471-2458-11-558.
65. Berg, B.L. 2001. *Qualitative Research Methods for the Social Sciences*. 7th ed. Boston, United States of America: Pearson.
66. Bhat, M. & Nelson, K.B. 1989. Developmental enamel defects in primary teeth in children with cerebral palsy, mental retardation, or hearing defects: a review. *Advances in Dental Research*. 3(2):132–142.
67. Biamino, E., Canale, A., Lacilla, M., Marinosci, A., Dagna, F., Genitori, L., Peretta,P., Silengo,M. et al. 2016. Prevention and management of hearing loss in syndromic craniosynostosis: a case series. *International Journal of Pediatric Otorhinolaryngology.* 85:95–98. doi: 10.1016/j.ijporl.2016.03.038.
68. Blachowska, E., Petriczko, E., Horodnicka-Józwa, A., Skórka, A., Pelc, M., Krajewska-Walasek, M.,Walczak, M. 2016. Recombinant growth hormone therapy in a girl with Costello syndrome: a 4-year observation. *Italian Journal of Pediatrics*. 42:10. doi:10.1186/s13052-015-0209-4.
69. Blazquez, E., Narvaez, D., Fernandez-Lopez, A., Garcia-Aparicio, L. 2016. Anesthetic management for thoracic surgery in Rubinstein-Taybi syndrome. *Revista Espanola de Anestesiologia Y Reanimacion*. 63(6):361–364. doi: 10.1016/j.redar.2016.02.004.

70. Bloch-Zupan, A., Stachtou, J., Emmanouil, D., Arveiler, B., Griffiths, D., Lacombe, D. 2007. Oro-dental features as useful diagnostic tool in Rubinstein-Taybi syndrome. *American Journal of Medical Genetics. Part A*. 143(6):570–573. doi:10.1002/ajmg.a.31622.

71. Boat, T. and Wu, J. 2015. *Mental disorders and disabilities among low-income children*. Washington, D.C.: National Academies Press.

72. Borland, L.M., Colligan, J. & Brandom, B.W. 2004. Frequency of anesthesia-related complications in children with Down syndrome under general anesthesia for noncardiac procedures. *Paediatric Anaesthesia*. 14(9):733–738. doi: 10.1111/j.1460-9592.2004.01329. x.

73. Bosshardt, D.D.2018. The periodontal pocket: pathogenesis, histopathology and consequences. Periodontology. 2000. 76 (1) 43–50. doi: 10.1111/prd.12153

74. Boulet, S.L., Schieve, L.A. & Boyle, C.A. 2011. Birth weight and health and developmental outcomes in us children, 1997-2005. *Maternal and Child Health Journal*. 15(7):836–844. doi:10.1007/s10995-009-0538-2.

75. Braddock, D., Emerson, E., Felce, D., Stancliffe, R.J. 2001. Living circumstances of children and adults with mental retardation or developmental disabilities in the United States, Canada, England and Wales, and Australia. *Mental Retardation and Developmental Disabilities Research Reviews*. 7(2):115–121. doi:10.1002/mrdd.1016.

76. Braddock, D., Hemp, R. & Rizzolo, M. 2004. State of the states in developmental disabilities: 2004. *Mental Retardation.* 42(5):357–370.

77. Brink, P.J. & Wood, M. 1998. *Advanced Design in Nursing Research*. 2nd ed, California, United States of America: SAGE Publications.

78. Brook, A.H. 2009. Multilevel complex interactions between genetic, epigenetic and environmental factors in the aetiology of anomalies of dental development. *Archives of Oral Biology*. 54 (Suppl 1):3-17. doi: 10.1016/j.archoralbio.2009.09.005.

79. Brown, K.A., Laferrière, A. & Moss, I.R. 2004. Recurrent hypoxemia in young children with obstructive sleep apnea is associated with reduced opioid requirement for analgesia. *Anesthesiology*. 100(4):806–810.

80. Bucsa, C., Moga, D.C., Farcas, A., Mogosan, C., Dumitrascu, D.L. 2015. An investigation of the concomitant use of angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and diuretics. *European Review for Medical and Pharmacological Sciences*. 19(15):2938–2944.

81. Buntinx, I.M., Hennekam, R.C., Brouwer, O.F., Stroink, H., Beuten, J., Mangelschots, K., Fryns, J.P. 1995. Clinical profile of Angelman syndrome at different ages. *American Journal of Medical Genetics*. 56(2):176–183. doi:10.1002/ajmg.1320560213.

82. Butler, M.G., Hayes, B.G., Hathaway, M.M., Begleiter, M.L. 2000. Specific genetic diseases at risk for sedation/anesthesia complications. *Anesthesia and Analgesia*. 91(4):837–855. doi:10.1097/00000539-200010000-00014.

83. Caballero, M.R., Tsabouri, S. & Dugue, P. 2009. Hypersensitivity to local anaesthetics - 6 facts and 7 myths. *Current Allergy and Clinical Immunology*. 22(3):117–120.
84. Cabrita, J.P., Bizarra, M. & Graça, S.R. 2017. Prevalence of malocclusion in individuals with and without intellectual disability: a comparative study. *Special Care in Dentistry*. 37(4):181–186. doi:10.1111/scd.12224.
85. Campos-Lara, P., Santos-Diaz, M., Ruiz-Rodríguez, M.S., Garrocho-Rangel, J.A., Pozos-Guillén, A.J. 2012. Orofacial findings and dental management of Williams-Beuren syndrome. *Journal of Clinical Pediatric Dentistry*. 36(4):401–404.
86. Carpentier, S., Schoenaers, J., Carels, C., Verdonck, A. 2014. Cranio-maxillofacial, orthodontic and dental treatment in three patients with Apert syndrome. *European Archives of Paediatric Dentistry.* 15(4):281–289. doi: 10.1007/s40368-013-0105-9.
87. Cassidy, J.P., Phero, J.C. & Grau, W.H. 1986. Epinephrine: systemic effects and varying concentrations in local anesthesia. *Anesthesia Progress*. 33(6):289–297.
88. Cauwels, R.G.E.C., De Coster, P.J., Mortier, G.R., Marks, L.A.M., Martens, L.C. 2005. Dentinogenesis imperfecta associated with short stature, hearing loss and mental retardation: a new syndrome with autosomal recessive inheritance? *Journal of Oral Pathology & Medicine*. 34(7):444–446. doi:10.1111/j.1600-0714.2005.00318. x.
89. Centres for Disease Control. 1986. *CDC infection control for dentists*. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/00033634.htm [2015, April 14].
90. Centres for Disease Control and Prevention.2015. Fetal Alcohol Syndrome Among Children Aged 7–9 Years — Arizona, Colorado, and New York, 2010.*Morbidity and Mortality Weekly Report.* 64(03):54-57. [Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6403a2.htm?s_cid=mm6403a2_w]
91. Chan, H.C., Estrella, N.M.R.P., Milkovich, R.N., Kim, J.W., Simmer, J.P.,Hu, J.C.C. 2011. Target gene analyses of 39 amelogenesis imperfecta kindreds. *European Journal of Oral Sciences.* 119. (Suppl.1):311–323. doi:10.1111/j.1600-0722.2011.00857. x.
92. Chandra, R.1997. Nutrition and the immune system: an introduction. American *Journal of Clinical Nutrition.*66(2): 460S-463S
93. Chang, H.P., Tseng, Y.C. & Chang, H.F. 2006. Treatment of mandibular prognathism. *Journal of the Formosan Medical Association*. 105(10):781–790. doi: 10.1016/S0929-6646(09)60264-3.
94. Chapple, I.L.C., Bouchard, P., Cagetti, M.G., Campus, G., Carra, M.C., Cocco, F., Nibali, L., Hujoel, P.,et. al. 2017. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint efp/orca workshop on the boundaries between caries and periodontal diseases. *Journal of Clinical Periodontology*. 44(Suppl 18):39–51. doi:10.1111/jcpe.12685.
95. Chaudhary, N., Ahlawat, B. & Kumar, A. 2015. Factors affecting children' s behaviour in the dental office. *Journal of Pharmaceutical and Biomedical Sciences.* 5(12):914–918

96. Chee, B., Park, B., Bartold, P.M., 2013. Periodontitis and type II diabetes: a two-way relationship. *International Journal of Evidence Based Healthcare*. 11(4): 317–329.
97. Chen, F., Li, Q., Gu, M., Li, X., Yu, J., Zhang, Y.B. 2015. Identification of a mutation in *FGF23* involved in mandibular prognathism. *Scientific Reports*. 5:11250. doi: 10.1038/srep11250.
98. Chen, J.C., Jen, R.K., Hsu, Y.W., Ke, Y.B., Hwang, J.J., Wu, K.H.,Wei, T.T. 1994. [4P- syndrome (Wolf-Hirschhorn syndrome) complicated with delay onset of malignant hyperthermia: a case report]. [Abstract]. *Acta Anaesthesiologica Sinica*. 32(4):275–278.
99. Chetty,M., Roberts, T.S., Stephen, L.X., Beighton, P.2017. Craniofacial manifestations in osteogenesis imperfecta type III in South Africa. *BDJ Open*. 17021 (2017). doi:10.1038/bdjopen.2017.21
100. Chikte, U.M., Gugushe, T.S., Rudolph, M.J., Reinach, S.G. 1990. Dental caries prevalence and CPITN of 12-year-old rural schoolchildren in Transkei. *South African Dental Journa*l. 45(6):245–249.
101. Choi, J.W., Kim, E.J., Min, B.W., Ban, J.S., Lee, S.G., Lee, J.H. 2012. Experience of severe desaturation during anesthetic induction period in an obese adult patient with Prader-Willi syndrome -A case report-. *Korean Journal of Anesthesiology*. 62(2):179–183. doi: 10.4097/kjae.2012.62.2.179.
102. Christianson, A.L., Zwane, M.E., Manga, P., Rosen, E., Venter, A., Downs, D., Kromberg, J.G.R. 2002. Children with intellectual disability in rural South Africa: prevalence and associated disability. *Journal of Intellectual Disability Research.*46(Pt 2):179–186.
103. Cleaton-Jones, P. & Fatti, P. 2009. Dental caries in children in South Africa and Swaziland: a systematic review 1919–2007. *International Dental Journal*. 59(6):363–368. doi: 10.1922/IDJ.
104. Cogulu, D., Sabah, E., Kutukculer, N., Ozkinay, F. 2006. Evaluation of the relationship between caries indices and salivary secretory IgA, salivary pH, buffering capacity and flow rate in children with Down's syndrome. *Archives of Oral Biology*. 51(1):23–28. doi: 10.1016/j.archoralbio.2005.06.001
105. Cogulu, D., Oncag, O., Celen, E., Ozkinay, F. 2008. Kabuki syndrome with additional dental findings: a case report. *Journal of Dentistry for Children*. 75(2):185–187.
106. Cogulu, D., Hazan, F. & Dindaroglu, F.C. 2015. Orofacial findings and dental management of Williams syndrome.*Genetic Counseling*. 26(4):437–442.
107. Coucouvanis, K., Lakin, K.C., Prouty, R., Webster, A. 2006. Reductions continue in average daily populations of large state facilities; nearly 70% decrease between 1980 and 2005. Mental Retardation. 44(3):235–238.
108. Couper, J. 2002. Prevalence of childhood disability in rural Kwazulu-Natal. *South African Medical Journal*. 92:549–552. doi:10.1093/annonc/mdt428.
109. Creswell, J.W. 2013. *Research Design: Qualitative, Quantitative and Mixed Methods Approaches*. 4th ed. California, United States of America: SAGE Publications,.
110. Cruz, R.M., Krieger, H., Ferreira, R., Mah, J., Hartsfield, J., Oliveira, S. 2008. Major gene and multifactorial inheritance of mandibular prognathism. *American Journal of Medical Genetics. Part A*. 146(1):71–77. doi: 10.1002/ajmg.a.32062.

111. Cumella, S., Ransford, N., Lyons, J., Burnham, H. 2000. Needs for oral care among people with intellectual disability not in contact with Community Dental Services. *Journal of Intellectual Disability Research.* 44 (Pt 1):45–52

112. Darrigo, L.G., Rodrigues, M.C., Pieroni, F., Stracieri, A.B.P.L., Moraes, D.A., Grecco, C.E.S., Dias, J.B.E., Sobral, A.C., et al. 2014. Successful outcome of allogeneic stem cell transplantation in Seckel syndrome. *Pediatric Transplantation*. 18(3):E93–E95. doi:10.1111/petr.12230.

113. Das, U.M., Beena, J.P. & Azher, U. 2009. Oral health status of 6- and 12-year-old school going children in Bangalore city: an epidemiological study. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 27(1):6–8. doi: 10.4103/0970-4388.50809.

114. Dawoud, B.E.S., Roberts, A. & Yates, J.M. 2014. Drug interactions in general dental practice - considerations for the dental practitioner. *British Dental Journal*. 216(1):15–23. doi: 10.1038/sj.bdj.2013.1237.

115. De Coster, P.J., Verbeeck, R.M.H., Holthaus, V., Martens, L.C., Vral, A. 2006. Seckel syndrome associated with oligodontia, microdontia, enamel hypoplasia, delayed eruption, and dentin dysmineralization: a new variant? *Journal of Oral Pathology & Medicine.* 35(10):639–641. doi:10.1111/j.1600-0714.2006.00462. x.

116. De Coster, P.J., Marks, L.A., Martens, L.C., Huysseune, A. 2009. Dental agenesis: genetic and clinical perspectives. *Journal of Oral Pathology and Medicine*. 38(1):1–17. doi:10.1111/j.1600-0714.2008.00699. x.

117. De Decker, R. & van der Merwe, E. 2011. Managing congenital heart disease and comorbidities - opening a pandora's box? *Continuing Medical Education*. 29(11/12):456. Available at: <http://www.cmej.org.za/index.php/cmej/article/view/2284/2049>.

118. de Freitas, M.R., Alcazar, N.M.P.V., Janson, G., de Freitas, K.M.S., Henriques, J.F.C. 2006. Upper and lower pharyngeal airways in subjects with Class I and Class II malocclusions and different growth patterns. *American Journal of Orthodontics and Dentofacial Orthopedics.* 130 (6): 742–745. doi: 10.1016/j.ajodo.2005.01.033

119. de Jong, T., Toll, M.S., de Gier, H.H.W. & Mathijssen, I.M.J. 2011. Audiological profile of children and young adults with syndromic and complex craniosynostosis. *Archives of Otolaryngology-Head & Neck Surgery*. 137(8):775–778. doi:10.1001/archoto.2011.115.

120. Dellavia, C., Allievi, C., Ottolina, P.,Sforza, C. 2009. Special care dentistry for people with intellectual disability in dental education: an Italian experience. *European Journal of Dental Education.* 13(4):218–222.

121. Della Marca, G., Rubino, M., Vollono, C., Vasta, I., Scarano, E., Mariotti, P., Cianfoni, A., Mennuni, G.F., et al. 2006. Rhythmic tongue movements during sleep: a peculiar parasomnia in Costello syndrome. *Movement Disorders*. 21(4):473–478. doi:10.1002/mds.20741.

122. Dellavia, C., Raiteri, S., Ottolina, P. & Pregliasco, F. 2011. Oral features in five adult patients with Wolf-Hirschhorn syndrome. *Minerva Stomatologica*. 60(7–8):391–402.

123. Delli, K., Reichart, P.A., Bornstein, M.M., Livas, C. 2013. Management of children with autism spectrum disorder in the dental setting: concerns, behavioural approaches and recommendations. *Medicina Oral, Patología Oral Y Cirugîa Bucal*. 18(6): e862-868.

124. Delsuc, F., Gasse, B. & Sire, J.Y. 2015. Evolutionary analysis of selective constraints identifies ameloblastin (*AMBN*) as a potential candidate for amelogenesis imperfecta. *BMC Evolutionary Biology*. 15:148. doi:10.1186/s12862-015-0431-0.

125. Department of Health South Africa. 2003. *National Policy for Oral Health in South Africa*. Available: https://www.westerncape.gov.za/text/2003/national_policy_oral_health_sa.pdf

126. Desai, M., Messer, L.B. & Calache, H. 2001. A study of the dental treatment needs of children with disabilities in Melbourne, Australia. *Australian Dental Journal*. 46(1):41–50. doi:10.1111/j.1834-7819. 2001.tb00273. x.

127. de Queiroz, A.M., de Siqueira Melara, T., Fernandes Ferreira, P.D., Lucisano, M.P., De Rossi, A., Nelson-Filho, P., Bezerra Silva, R.A. 2013. Dental findings and special care in patients with Angelman syndrome: a report of three cases. *Special Care in Dentistry.* 33(1):40–45. doi: 10.1111/j.1754-4505.2012.00292. x.

128. Detweiler, S., Thacker, M.M., Hopkins, E., Conway, L., Gripp, K.W. 2013. Orthopedic manifestations and implications for individuals with Costello syndrome. *American Journal of Medical Genetics, Part A*. 161(8):1940–1949. doi:10.1002/ajmg.a.36047.

129. de Vries, T.I., R Monroe, G., van Belzen, M.J., van der Lans, C.A., Savelberg, S.M., Newman, W.G., van Haaften, G., Nievelstein, R.A, et al. 2016. Mosaic *CREBBP* mutation causes overlapping clinical features of Rubinstein-Taybi and Filippi syndromes. *European Journal of Human Genetics.*24(9):1363-1366. doi:10.1038/ejhg.2016.14.

130. Diab, H.A., Salameh, Z., Hamadeh, G.N., Younes, G.,Ayoub, F. 2017. Oral health status of institutionalized individuals with intellectual disabilities in Lebanon. *Journal of Oral & Maxillofacial Research*. 8(1): e4. doi:10.5037/jomr.2017.8104.

131. Dietrich, T., Nunn, M., Dawson-Hughes, B., Bischoff-Ferrari, H. 2005. Association between serum concentrations of 25-hydroxyvitamin D and gingival inflammation. *American Journal of Clinical Nutrition*. 82(4):575–580.

132. Disha, P., Poornima, P., Pai, S.M., Nagaveni, N.B., Roshan, N.M., Manoharan, M. 2017. Malocclusion and dental caries experience among 8-9-year-old children in a city of South Indian region: A cross-sectional survey. *Journal of Education and Health Promotion.* 6: 98.

133. Dixit, S., Singh, A., Mamatha,G.S., Desai, R., Jaju, P. 2008. Apert syndrome: report of a new case and its management. *International Journal of Clinical Pediatric Dentistry*. 1(1):48–53. doi: 10.5005/jp-journals-10005-1009.

134. Dizdar, O., Baspınar, O., Kocer, D., Dursun, Z., Avcı, D., Karakükcü, C., Çelik, İ., Gundogan, K. 2016. Nutritional risk, micronutrient status and clinical outcomes: a prospective observational study in an infectious disease clinic. *Nutrients*. 8(3):124. doi: 10.3390/nu8030124.

135. do Prado Sobral, S., Leite, A.F., Figueiredo, P.T., Ferrari, I., Safatle, H.P., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al., 2013. Craniofacial and dental features in Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal.* 50(4):440–447. doi: 10.1597/11-052.
136. Domenico, S., Orlando, C., Graziana, F.F.M., Papi, P., Giulia, A. 2013. Cleft palate in Williams syndrome. *Annals of Maxillofacial Surgery*. 3(1):84–86. doi: 10.4103/2231-0746.110071.
137. Doruk, C., Bicakci, A.A. & Babacan, H. 2003. Orthodontic and orthopedic treatment of a patient with Incontinentia pigmenti. *Angle Orthodontist*. 73(6):763–768. doi:10.1043/0003-3219(2003)073<0763:OAOTOA>2.0.co.2
138. Doshi, D.C., Limdi, P.K., Parekh, N. V., Gohil, N.R. 2016. Oculodentodigital dysplasia. *Indian Journal of Ophthalmology*. 64(3):227–230. doi:10.4103/0301-4738.180191.
139. Dougall, A. & Fiske, J. 2008. Access to special care dentistry,Part 6. Special care dentistry services for young people. *British Dental Journal*. 205(5):235–249. doi: 10.1038/sj.bdj.2008.734.
140. Drugowick, R.M., Da Rós Gonçalves, L., Barrôso, A.S., Feres-Filho, E.J. & Maia, L.C. 2007. Treatment of gingival overgrowth in a child with Bardet-Biedl syndrome. *Journal of Periodontology*. 78(6):1159–1163. doi:10.1902/jop.2007.060378.
141. Duarte-Rodrigues, L., Ramos-Jorge, J., Drumond, C.L., Diniz, P.B., Marques, L.S., Ramos-Jorge, M.L. 2017. Correlation and comparative analysis of the CPQ8-10 and child-OIDP indexes for dental caries and malocclusion. *Brazil Oral Research.* 31, e111.
142. Dudovskiy, J. Ed. 2016. *An Ultimate Guide to Writing a Dissertation in Business Studies: A Step-by-Step Assistance*. Available: http://research-methodology.net/about-us/ebook/.
143. Dykens, E.M., Roof, E. & Hunt-Hawkins, H. 2017. Cognitive and adaptive advantages of growth hormone treatment in children with Prader-Willi syndrome. *Journal of Child Psychology and Psychiatry*. 58(1):64–74. doi:10.1111/jcpp.12601.
144. Elwood, T., Sarathy, P. V, Geiduschek, J.M., Ulma, G.A., Karl, H.W. 2001. Respiratory complications during anaesthesia in Apert syndrome. *Paediatric Anaesthesia*. 11(6):701–703. doi: 10.1046/j.1460-9592.2001.00745.x.
145. Emerson, E. 2004. Poverty and children with intellectual disabilities in the world's richer countries. *Journal of Intellectual & Developmental Disability*. 29 (4):319-338. doi:10.1080/13668250400014491
146. Evlice, B., Tatli, U., Yazicioglu, I., Evlice, A., Oztunc, H. 2013. A unique case of Turner syndrome accompanying prolactinoma and unexpected elongated styloid process: clinical and cone-beam computed tomographic features. *Imaging Science in Dentistry*. 43(2):129-134. doi:10.5624/isd.2013.43.2.129.
147. Fernandez, C., Declerck, D., Dedecker, M., Marks, L. 2015. Treatment needs and impact of oral health screening of athletes with intellectual disability in Belgium. *BMC Oral Health*. 15:170. doi: 10.1186/s12903-015-0157-9.
148. Fernandez, C., Descamps, I., Fabjanska, K., Kaschke, I. & Marks, L. 2016. Treatment needs and predictive capacity of explanatory variables of oral disease in young athletes with an intellectual disability in Europe and Eurasia. *European Journal of Paediatric Dentistry.* 17(1):9–16.

149. Fernandez, J.B., Lim, L.J., Dougherty, N., LaSasso, J., Atar, M., Daronch, M. 2012. Oral health findings in athletes with intellectual disabilities at the NYC Special Olympics. *Special Care in Dentistry.* 32(5):205–209. doi: 10.1111/j.1754-4505.2012.00268. x.

150. Ferreira do Amaral, C.O., Logar, Gde A., Parisi, A.G., Takahashi, K., Straioto, F.G. 2014. General and stomatologic aspects of Bardet-Biedl syndrome.*Journal of Craniofacial Surgery*. 25(6): e575–e578. doi:10.1097/scs.0000000000001169.

151. Ferrini, F.R.D., Marba, S.T.M. & Gavião, M.B.D. 2008. Oral conditions in very low and extremely low birth weight children. *Journal of Dentistry for Children*. 75(3):235–242.

152. Finucane, B.T. 2003. Allergies to local anesthetics - the real truth. *Canadian Journal of Anaesthesia*. 50(9):869–874. doi:10.1007/bf03018730.

153. Fitaw, Y. & Boersma, J.M.F. 2006. Prevalence and impact of disability in north-western Ethiopia. *Disability and Rehabilitation*. 28(15):949–953. doi:10.1080/09638280500404552.

154. Flaitz, C., Wullbrandt, B., Sexton, J., Bourdon, T., Hicks, J. 2001. prevalence of orodental findings in HIV-infected Romanian children. *Pediatric Dentistry*. 23(1):44–50.

155. Flint, J. 2001. Genetic basis of cognitive disability. *Dialogues in Clinical Neuroscience*. 3(1):37–46.

156. Forsythe, E., Sparks, K., Best, S., Borrows, S., Hoskins, B., Sabir, A., Barrett, T., Williams, D., et al. 2017. Risk factors for severe renal disease in Bardet–Biedl syndrome. *Journal of the American Society of Nephrology*. 28(3):963–970. doi:10.1681/asn.2015091029.

157. Foster, S.C. 1971. Prader-Willi syndrome: report of cases. *Journal of the American Dental Association*. 83(3):634–638.

158. Friedling, L.J. & Morris, A.G. 2005. The frequency of culturally derived dental modification practices on the Cape flats in The Western Cape. *South African Dental Journal*. 60(3):97, 99–102.

159. Friedling, L.J. & Morris, A.G. 2007. Pulling teeth for fashion: dental modification in modern day Cape Town, South Africa. *South African Dental Journal*. 62(3):106, 108–113.

160. Frydman, A. & Nowzari, H. 2012. Down syndrome-associated periodontitis: a critical review of the literature. *Compendium of Continuing Education in Dentistry*. 33(5):356–361.

161. Gadiwalla, Y., Burnham, R., Warfield, A., Praveen, P. 2016. Surgical Management of macroglossia secondary to amyloidosis. *BMJ Case Reports*. 2016. doi:10.1136/bcr-2015-214078.

162. Gajula, P., Ramalingam, K. & Bhadrashetty, D. 2012. A rare case of mucopolysaccharidosis: Hunter syndrome. *Journal of Natural Science, Biology, and Medicine*. 3(1):97–100. doi:10.4103/0976-9668.95984.

163. Gallo, C., Marcato, A., Beghetto, M., Stellini, E. 2012. dental treatment in Angelman Syndrome patients. 8 case reports. *European Journal of Paediatric Dentistry.* 13(4):345–348.

164. Galluccio, G., Castellano, M. & La Monaca, C. 2012. Genetic basis of non-syndromic anomalies of human tooth number. *Archives of Oral Biology*. 57(7):918–930. doi: 10.1016/j.archoralbio.2012.01.005.

165. Ganzberg, S. 2016. Obstructive sleep apnea and office-based surgery. *Anesthesia Progress*. 63(2):53–54. doi:10.2344/0003-3006-63.2.53.

166. Gao, X., Hamzah, S.H., Yiu, C.K.Y., McGrath, C.,King, N.M. 2013. Dental fear and anxiety in children and adolescents: qualitative study using Youtube. *Journal of Medical Internet Research*. 15(2):e29. doi:10.2196/jmir.2290.

167. Gardens, S.J., Krishna, M., Vellappally, S., Alzoman, H., Halawany, H.S., Abraham, N.B. & Jacob, V. 2013. Oral health survey of 6-12-year-old children with disabilities attending special schools in Chennai, India. *International Journal of Paediatric Dentistry*.24(6): 424–433. doi:10.1111/ipd.12088.

168. Gardner, D.G. 1968. Metachromatic cells in the gingiva in Hurler's syndrome. *Oral Surgery, Oral Medicine and Oral Pathology*. 26(6):782–789.

169. Garg, R., Uppal, S., Mittal, R., Grewal, A., Sood, D.,Shah, S. 2012. Palatoplasty in a patient with Seckel syndrome. *Annals of Maxillofacial Surgery*. 2(1):63–65. doi: 10.4103/2231-0746.95324.

170. General Dental Council. Standards for Dental Professionals.2005. London: The General. Dental Council.

171. George, A., Johnson, M., Blinkhorn, A., Ajwani, S., Ellis, S., Bhole, S. 2013. Views of pregnant women in South Western Sydney towards dental care and an oral-health program initiated by midwives. *Health Promotion Journal of Australia*. 24(3):178. doi: 10.1071/HE13040.

172. Ghafournia, M. & Hajenourozali Tehrani, M.2012. Relationship between Bruxism and Malocclusion among Preschool Children in Isfahan. *Journal of Dental Research, Dental Clinics, Dental Prospects*. 6(4): 138–142. doi:10.5681/joddd.2012.028

173. Ghiz, M.A., Ngan, P.& Gunel, E., 2005. Cephalometric variables to predict future success of early orthopedic Class III treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*. 127 (3):301–306. doi: 10.1016/j.ajodo.2004.02.014

174. Gomes, M.C., Pinto-Sarmento, T.C., Costa, E.M.M., Martins, C.C., Granville-Garcia, A.F. & Paiva, S.M. 2014. Impact of oral health conditions on the quality of life of preschool children and their families: a cross-sectional study. *Health and Quality of Life Outcomes*. 12:55. doi:10.1186/1477-7525-12-55.

175. Gomes-Silva, J.M., Ruviere, D.B., Segatto, R.A., de Queiroz, A.M.,de Freitas, A.C. 2006. Sotos syndrome: a case report. *Special Care in Dentistry*. 26(6):257–262.

176. Goodwin, A.F., Oberoi, S., Landan, M., Charles, C., Massie, J.C., Fairley, C., Rauen, K.A.,Klein, O.D. 2014. Craniofacial and dental development in Costello syndrome. *American Journal of Medical Genetics Part A*. 164(6):1425–1430. doi:10.1002/ajmg.a.36475.

177. Grantham-McGregor, S. & Baker-Henningham, H. 2005. Review of the evidence linking protein and energy to mental development. *Public Health Nutrition*. 8(7A):1191–1201.

178. Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L.,Strupp, B.2007. Developmental potential in the first 5 years for children in developing countries.*Lancet.* 369(9555):60-70. doi: 10.1016/S0140-6736(07)60032-4

179. Grewal, A., Sood, D., Bhatia, N., Garg, R., Shah, S. & Kaur, H. 2014. Palatoplasty in a patient with Seckel syndrome: an anesthetic challenge. *Brazilian Journal of Anesthesiology*. 64(3):216–218. doi: 10.1016/j.bjane.2013.08.005.

180. Grugni, G., Sartorio, A. & Crinò, A. 2016. Growth hormone therapy for Prader-Willi syndrome: challenges and solutions. *Therapeutics and Clinical Risk Management*. 12:873-881. doi:10.2147/tcrm.s70068.

181. Guan, X., Song, Y., Ott, J., Zhang, Y., Li, C., Xin, T., Li, Z., Gan, Y., et al., 2015. The *ADAMTS1* gene is associated with familial mandibular prognathism. *Journal of Dental Research*. 94(9):1196–1201. doi: 10.1177/0022034515589957.

182. Guimaraes, C.V.A., Donnelly, L.F., Shott, S.R., Amin, R.S., Kalra, M. 2008. Relative rather than absolute macroglossia in patients with Down syndrome: implications for treatment of obstructive sleep apnea. *Pediatric Radiology*. 38(10):1062–1067. doi:10.1007/s00247-008-0941-7.

183. Gurumurthy, T., Shailaja, S., Kishan, S., Stephen, M. 2014. Management of an anticipated difficult airway in Hurler's syndrome. *Journal of Anaesthesiology, Clinical Pharmacology*. 30(4):558–561. doi: 10.4103/0970-9185.142862.

184. Guven, G., Cehreli, Z.C., Altun, C., Şençimen, M., Ide, S., Bayari, S.H., Karaçay, Ş,. 2008. Mucopolysaccharidosis type I (Hurler syndrome): oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*. 105(1):72–78. doi: 10.1016/j.tripleo.2007.02.015.

185. Haas, D.A., Young, E.R. & Harper, D.G. 1992. Malignant hyperthermia and the general dentist: current recommendations. *Journal of the Canadian Dental Association*. 58(1):28–33.

186. Hahn, J.S. & Hanauer, A. 2012. Stimulus-induced drop episodes in Coffin-Lowry syndrome. *European Journal of Medical Genetics*. 55(5):335–337. doi: 10.1016/j.ejmg.2012.03.004.

187. Hamilton-Craig, I. 2001. Statin-associated myopathy. *Medical Journal of Australia*. 175(9): 486-489.doi:10.1001/jama.289.13.1681.

188. Hanauer, A. & Young, I. 2002. Coffin-Lowry Syndrome: clinical and molecular features. *Journal of Medical Genetics*. 77(10):705–713. doi:10.1136/jmg.39.10.705.

189. Harris, J. 2006. Intellectual disability: understanding its development, causes, classification, evaluation , and treatment. *Oxfort University Press*.

190. Harsha Vardhan, B.G., Muthu, M.S., Saraswathi, K., Koteeswaran, D.2007. Bird-headed dwarf of Seckel. *Journal of the Indian Society of Pedodontics and Preventative Dentistry*. 25(5):8–9.

191. Hartsfield, J.K., Hall, B.D., Grix, A.W., Kousseff, B.G., Salazar, J.F., Haufe, S.M. 1993. Pleiotropy in Coffin-Lowry syndrome: sensorineural hearing deficit and premature tooth loss as early manifestations. *American Journal of Medical Genetics*. 45(5):552–557. doi:10.1002/ajmg.1320450505.

192. Hasan, A. & Palmer, R.M. 2014. A clinical guide to periodontology: pathology of periodontal disease. *British Dental Journal*. 216(8):457–461. doi: 10.1038/sj.bdj.2014.299.

193. Hasslöf, P. & Twetman, S. 2007. Caries prevalence in children with cleft lip and palate--a systematic review of case-control studies. *International Journal of Paediatric Dentistry.* 17(5):313–319. doi: 10.1111/j.1365-263X.2007.00847.x.

194. Hegde, A.M., Kavita, R., Sushma, K.S., Suchetha, S. 2012. Salivary sialic acid levels and dental health in children with congenital heart disease. *Journal of Clinical Pediatric Dentistry*. 36(3):293–296.

195. Hennekam, R.C. & Van Doorne, J.M. 1990. Oral aspects of Rubinstein-Taybi syndrome. *American Journal of Medical Genetics.* 36(Suppl 6):42–47.

196. Hennekam, R.C.M. 2003. Costello syndrome: an overview. *American Journal of Medical Genetics. Part C.* 117(1):42–48. doi:10.1002/ajmg.c.10019.

197. Henneman, A. & Thornby, K.A. 2012. Risk of hypotension with concomitant use of calcium-channel blockers and macrolide antibiotics. *American Journal of Health-System Pharmacy*. 69(12):1038–1043. doi:10.2146/ajhp110486.

198. Hertzberg, J., Nakisbendi, L., Needleman, H.L.., Pober, B. 1994. Williams syndrome--oral presentation of 45 cases. *Pediatric Dentistry*. 16(4):262–267.

199. Higashi, K. & Matsuki, C. 1994. Coffin-Lowry syndrome with sensorineural deafness and labyrinthine anomaly. *Journal of Laryngology and Otology*. 108(2):147–148.

200. Hirai, N., Matsune, K. & Ohashi, H. 2011. Craniofacial and oral features of Sotos syndrome: differences in patients with submicroscopic deletion and mutation of *NSD1* gene. *American Journal of Medical Genetics.Part A*. 155(12):2933–2939. doi:10.1002/ajmg.a.33969.

201. Holt, K. & Kraft, K. 2010. Oral health and learning. *Journal of the Oklahoma Dental Association*. 97(1):24–25.

202. Houpt, M.I., Sheskin, R.B., Koenigsberg, S.R., Desjardins, P.J., Shey, Z. 1985. Assessing chloral hydrate dosage for young children. *Pediatric Dentistry*: 7(1):41-46. Available: http://www.ncbi.nlm.nih.gov/pubmed/3862684 [2016, December 01].

203. Huh, R., Cho, S.Y., Kim, J., Ki, C.S., Jin, D.K. 2015. A novel mutation in the *CREBBP* gene of a Korean girl with Rubinstein-Taybi syndrome. *Annals of Clinical and Laboratory Science*. 45(4):458–461.

204. Hujoel, P.P. & Lingström, P. 2017. Nutrition, dental caries and periodontal disease: a narrative review. *Journal of Clinical Periodontology*. 44 (Suppl 18):79–84. doi:10.1111/jcpe.12672.

205. Huston, A.C., McLoyd, V.C. & Coll, C.G. 1994. Children and poverty: issues in contemporary research. *Child Development*. 65(2):275–282. doi:10.1111/1467-8624.ep9405315099.

206. Iida, T., Park, S., Kato, K., Kitano, I. 2006. Cleft palate in Kabuki syndrome: a report of six cases. *Cleft Palate-Craniofacial Journal.* 43(6):756–761. doi: 10.1597/05-174.

207. Imataka, G., Nakajima, I., Goto, K., Konno, W., Hirabayashi, H., Arisaka, O. 2016. Drop episodes improved after tracheotomy: a case of Coffin-Lowry syndrome associated with obstructive sleep apnea syndrome. *European Review for Medical and Pharmacological Sciences*. 20(3):498–501.

208. Inokuchi, M., Nomura, J., Mtsumura, Y., Sekida, M., Tagawa, T. 2001. Sotos syndrome with enamel hypoplasia: a case report. *Journal of Clinical Pediatric Dentistry*. 25(4):313–316.

209. Ioannou, S., Sassani, S., Henneberg, M. & Henneberg, R.J. 2016. Diagnosing congenital syphilis using Hutchinson's method: differentiating between syphilitic, mercurial, and syphilitic-mercurial dental defects. *American Journal of Physical Anthropology*. 159(4):617–629. doi:10.1002/ajpa.22924.

210. Ireland, W. 1882. On the diagnosis and prognosis of idiocy. *Edinburgh Medical Journal*. 1072–1085.

211. Jabbari, F., Reiser, E., Thor, A., Hakelius, M., Nowinski, D. 2016. Correlations between initial cleft size and dental anomalies in unilateral cleft lip and palate patients after alveolar bone grafting. *Upsala Journal of Medical Sciences*. 121(1):33–37. doi: 10.3109/03009734.2015.1134733.

212. Jaccarino, J. 2009. General treatment considerations for the patient with special needs. *Dental Assistant*. 78:6–9, 34–36.

213. Jacobs, I.N., Gray, R.F. & Todd, N.W. 1996. Upper airway obstruction in children with Down syndrome. *Archives of Otolaryngology-Head & Neck Surgery*. 122(9):945–950.

214. Jay, V., Becker, L.E., Chan, F.W., Perry, T.L. 1991. Puppet-like syndrome of Angelman: a pathologic and neurochemical study. *Neurology*. 41(3):416–422.

215. Jeon, J., Kim, J.H. & Oh, C.H. 2014. Trichorhinophalangeal syndrome Type I: clinical, microscopic, and molecular features. *Indian Journal of Dermatology, Venereology and Leprology*. 80(1):54–57. doi:10.4103/0378-6323.125515.

216. Johnson, B.A., Dajnoki, A. & Bodamer, O.A. 2015. Diagnosing lysosomal storage disorders: mucopolysaccharidosis type I. *Current Protocols in Human Genetics*. 84.17(17):1-.8. doi:10.1002/0471142905.hg1717s84.

217. Johnston, N.J. & Franklin, D.L. 2006. Dental findings of a child with Wolf-Hirschhorn syndrome. *International Journal of Paediatric Dentistry.* 16(2):139–142. doi:10.1111/j.1365-263x.2006.00675. x.

218. Jones, D. & Morrison, J. 2016. Preventative therapies and periodontal interventions for Down syndrome patients. *Evidence-Based Dentistry*. 17(4):101–102. doi: 10.1038/sj.ebd.6401198.

219. Jose, R., Chandra, S., Puttabuddi, J.H., Vellappally, S., Al Khuraif, A.-A.A., Halawany, H.S., Abraham, N.B., Jacob, V., et al. 2013. Prevalence of oral and systemic manifestations in pediatric HIV cohorts with and without drug therapy. *Current HIV Research*. 11(6):498–505.

220. Joseph, C., Landru, M.M., Bdeoui, F., Gogly, B., Dridi, S.M. 2008. Periodontal conditions in Williams Beuren syndrome: a series of 8 cases. *European Archives of Paediatric Dentistry.* 9(3):142–147.

221. Joshi, S.R., Pendyala, G.S., Saraf, V., Choudhari, S., Mopagar, V., 2013. A comprehensive oral and dental management of an epileptic and intellectually deteriorated adolescent. *Dental Research Journal.* 10(4): 562–567.

222. Joshipura, K.J., Muñoz-Torres, F.J., Dye, B.A., Leroux, B.G., Ramírez-Vick, M., Pérez, C.M. 2018. Longitudinal Association between Periodontitis and Development of Diabetes.*Diabetes Research and Clinical Practice.* doi: 10.1016/j.diabres.2018.04.028

223. Kamenarova, K., Simeonov, E., Tzveova, R., DachevaD., Penkov M., Kremensky, I., Perenovska, P., Mitev, V, K.R. 2016. Identification of a novel de novo mutation of *CREBBP* in a patient with Rubinstein-Taybi syndrome by targeted next-generation sequencing: a case report. *Human Pathology.* 47(1):144–149. doi: 10.1016/j.humpath.2015.09.004.
224. lirk, W. 2008. Diagnosis and management of respiratory involvement in Hunter syndrome. *Acta Paediatrica*. 97(Suppl 457):57–60. doi: 10.1111/j.1651-2227.2008.00650. x.
225. Karaer, K. & Yüksel, Z. 2014. Tricho-rhino-phalangeal Syndrome type 1 as an outcome of in vitro fertilization? *Genetic Counseling*. 25(1):13–17.
226. Karahan, M.A., Sert, H., Ayhan, Z., Ayhan, B. 2016. Anaesthetic management of children with Rubinstein-Taybi syndrome. *Turkish Journal of Anaesthesiology and Reanimation*. 44(3):152–154. doi:10.5152/tjar.2016.76992.
227. Kariya, S., Schachern, P.A., Nishizaki, K., Paparella, M.M., Cureoglu, S. 2012. Inner ear changes In Mucopolysaccharidosis Type I /Hurler Syndrome. *Otology & Neurotology*. 33(8):1323–1327. doi: 10.1097/mao.0b013e3182659cc3.
228. Karnosh, J. 1926. Histopathology of syphilitic hypoplasia of the teeth. *Archives of Dermatology and Syphilology*. 13(1):25–42.
229. Katcher, K., Bothwell, M. & Tobias, J.D. 2003. Anaesthetic implications of Costello syndrome. *Paediatric Anaesthesia*. 13(3):257–262.
230. Kaur, S., White, S. & Bartold, M. 2012. Periodontal disease as a risk factor for rheumatoid arthritis: a systematic review. *JBI Database of Systematic Reviews and Implementation Reports*. 10 (41. Suppl):1–12. doi:10.11124/jbisrir-2012-288.
231. Kechaou, I., Cherif, E., Ben Hassine, L., Khalfallah, N. 2014. Liver involvement in tuberous sclerosis. *BMJ Case Reports*. 2014. doi:10.1136/bcr-2013-201650.
232. Khalaf, K., Miskelly, J., Voge, E.,Macfarlane, T. V. 2014. Prevalence of hypodontia and associated factors: a systematic review and meta-analysis. *Journal of Orthodontics*. 41(4):299–316. doi:10.1179/1465313314y.0000000116.
233. Khan, M.A., Addison, O., James, A., Hendriksz, C.J. & Al-Jawad, M. 2017. Synchrotron X-ray diffraction to understand crystallographic texture of enamel affected by Hunter syndrome. *Archives of Oral Biology*. 80:193–196. doi: 10.1016/j.archoralbio.2017.04.019.
234. Khan, S., Chatra, L., Shenai, P., Veena, K. 2012. Apert syndrome: a case Report. *International Journal of Clinical Pediatric Dentistry*. 5(3):203–206. doi: 10.5005/jp-journals-10005-1166.
235. Khodadadi, E., Niknahad, A., Sistani, M.M.N. & Motallebnejad, M. 2016. Parents' oral health literacy and its impact on their children's dental health status. *Electronic Physician*. 8(12):3421–3425. doi: 10.19082/3421.
236. Kirchberg, A., Treide, A. & Hemprich, A. 2004. Investigation of caries prevalence in children with cleft lip, alveolus, and palate. *Journal of Cranio-Maxillo-Facial Surgery.* 32(4):216–219. doi: 10.1016/j.jcms.2004.02.003.

237. Kitakawa, D., Fontes, P.C., Magalhães, F.A.C., Almeida, J.D.,Cabral, L.A.G. 2009. Incontinentia pigmenti presenting as hypodontia in a 3-year-old girl: a case report. *Journal of Medical Case Reports*. 3:116. doi:10.1186/1752-1947-3-116.

238. Kleint, G., Kanitz, G. & Harzer, W. 2002. Orthodontic treatment in handicapped children: report of four cases. *ASDC Journal of Dentistry for Children*. 69(1):11,31-38.

239. Kleintjes, S., Flisher, A.J., Fick, M., Railoun, A., Lund, C., Molteno, C., Robertson, B.A. 2006. The prevalence of mental disorders among children, adolescents and adults in the Western Cape, South Africa. *South African Psychiatry Review*. 9:157–160. doi:10.4314/ajpsy. v9i3.30217.

240. Klingberg G.2008. Dental anxiety and behaviour management problems in paediatric dentistry:a review of the background factors and diagnostics. *European Archives of Paediatric Dentistry.*9 (Suppl 1):11-15

241. Knoll-Köhler, E., Frie, A., Becker, J., Ohlendorf, D. 1989. Changes in plasma epinephrine concentration after dental infiltration anesthesia with different doses of epinephrine. *Journal of Dental Research*. 68(6):1098–1101.

242. Knopp, C., Rudnik-Schöneborn, S., Zerres, K., Gencik, M., Spengler, S., Eggermann, T. 2015. Twenty-one years to the right diagnosis - clinical overlap of Simpson-Golabi-Behmel and Beckwith-Wiedemann syndrome. *American Journal of Medical Genetics. Part A*. 167(1):151–155. doi:10.1002/ajmg.a.36825.

243. Kobayashi, E.T., Maruyama, Y. & Kobayashi, K. 2001. A longitudinal evaluation of craniofacial growth in a patient with Kabuki Make-up syndrome: a case report. *European Journal of Orthodontics*. 23(2):205–213.

244. Kobrin, J.L., Ternand, C.L., Knobloch, W.H.,Johnson, D.D. 1990. Dental abnormalities as a component of the Laurence-Moon-Bardet-Biedl syndrome. *Ophthalmic Paediatrics and Genetics*. 11(4):299–303.

245. Koike, S., Sujino, T., Ohmori, H., Shimazaki, K., Fukuyama, E., Kanai, T., Hibi, T., Ono, T. 2013. Gastric emptying rate in subjects with malocclusion examined by [(13) C] breath test. Journal of Oral Rehabilitation. 40(8): 574–581. doi:10.1111/joor.12073

246. Komura Y, Kaga K, Ogawa Y, Yamaguchi Y, Tsuzuku T, S.J. 1998. ABR and temporal bone pathology in Hurler's disease. *Internal Journal of Pediatric Otorhinolaryngology.* 43(2):179–188.

247. Kondo, S., Okuyama, K., Ikemoto, K., Furuya, A.,Matsukawa, T. 2013. General anesthesia for a boy with Wolf-Hirschhorn syndrome. *Japanese Journal of Anesthesiology*. [Abstract] 62(12):1466–1468.

248. Kovac, M., Mitic, G. & Kovac, Z. 2012. Miconazole and nystatin used as topical antifungal drugs interact equally strongly with warfarin. *Journal of Clinical Pharmacy and Therapeutics*. 37(1):45–48. doi:10.1111/j.1365-2710.2011.01246. x.

249. Krasuski, R.A., Bashore, T.M., Warnes, C., Williams, R., Bashore, T., Child, J., Connolly, H., Dearani, J., et al. 2016. Congenital heart disease epidemiology in the United States: blindly feeling for the charging elephant. *Circulation*. 134(2):110–113. doi:10.1161/circulationaha.116.023370.

250. Krimmel, M. & Reinert, S. 2000. Multiple odontogenic keratocysts in Mental Retardation-Overgrowth (Simpson-Golabi-Behmel) syndrome. *British Journal of Oral & Maxillofacial Surgery*. 38(3):221–223. doi: 10.1054/bjom.1999.0186.

251. Kromberg, J., Zwane, E., Manga, P., Venter, A., Rosen, E., Christianson, A. 2008. Intellectual disability in the context of a South African population. *Journal of Policy Practice in Intellectual Disabilities*. 5(2):89–95. doi:10.1111/j.1741-1130.2008.00153. x.

252. Kumar, N., Arora, S., Bindra, A. & Goyal, K. 2014. Anesthetic management of craniosynostosis repair in patient with Apert syndrome. *Saudi Journal of Anaesthesia*. 8(3):399–401. doi: 10.4103/1658-354X.136631.

253. Kumar, P., Mastan, K.M.K., Chowdhary, R., Shanmugam, K., 2012. Oral manifestations in hypertensive patients: A clinical study. *Journal of Oral Maxillofacial Pathology.* 16(2): 215. doi.10.4103/0973-029X.99069

254. Kumar, S., Sharma, J., Duraiswamy, P., Kulkarni, S. 2009. Determinants for oral hygiene and periodontal status among mentally disabled children and adolescents. *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 27(3):151-157. doi: 10.4103/0970-4388.57095

255. Legrand, R. & Tobias, J.D. 2006. Anesthesia and Prader-Willi syndrome: preliminary experience with regional anesthesia. *Paediatric Anaesthesia*. 16(7):712–722. doi: 10.1111/j.1460-9592.2006.01968. x.

256. Leonard, H. and Wen, X.2002. The epidemiology of mental retardation: challenges and opportunities in the new millennium. Mental Retardation and Developmental Disabilities. 2002;8(3):117-134

257. Leroy, R., Declerck, D. & Marks, L. 2012. The oral health status of Special Olympics athletes in Belgium. *Community Dental Health*. 29(1):68–73.

258. Lesperance, M.M., Grundfast, K.M.,Rosenbaum, K.N. 1998. Otologic manifestations of Wolf-Hirschhorn syndrome. *Archives of Otolaryngology--Head & Neck Surgery*. 124(2):193–196.

259. Letra, A., de Almeida, A.L., Kaizer, R., Esper, L.A., Sgarbosa, S., Granjeiro, J.M. 2007. Intraoral features of Apert's syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 103(5): e38-41. doi: S1079-2104(06)00287-3.

260. Lewis, D.D., Shaffer, J.R., Feingold, E., Cooper, M., Vanyukov, M.M., Maher, B.S. Slayton, R L. & et al. 2017. Genetic Association of MMP10, MMP14, and MMP16 with Dental Caries. *International Journal of Dentistry.* 2017, Article ID 8465125, 7 pages. doi.org/10.1155/2017/8465125

261. Limeres Posse, J., López Jiménez, J., Ruiz Villandiego, J.C., Cutando Soriano, A., Fernández Feijoo, J., Linazasoro Elorza, M., Diniz Freitas, M., Diz Dios, P. 2016. Survival of dental implants in patients with Down syndrome: a case Series. *Journal of Prosthetic Dentistry*. 116(6):880–884. doi: 10.1016/j.prosdent.2016.04.015.

262. Lirk, P., Keller, C., Colvin, J., Rieder, J., Wulf, K. 2004. Anaesthetic management of the Prader-Willi syndrome. *European Journal of Anaesthesiology*. 21(10):831–833.

263. Liu, H.Y., Chen, C.C., Hu, W.C., Tang, R.C., Chen, C.C., Tsai, C.C. & Huang, S. T. 2010. The impact of dietary and tooth-brushing habits to dental caries of special school children with disability. *Research in Developmental Disabilities*. 31(6):1160–1169. doi: 10.1016/j.ridd.2010.08.005.

264. Lodi, M., Chifari, R., Parazzini, C., Viri, M., Beccaria, F., Lorenzetti, M.E., Meloni, M., Capovilla, G., et al. 2010. Seizures and EEG pattern in Kabuki syndrome. *Brain & Development*. 32(10):829–834. doi: 10.1016/j.braindev.2009.12.006.

265. Lucea, M.B., Stockman, J.K., Mana-Ay, M., Bertrand, D., Callwood, G.B., Coverston, C.R., Campbell, D.W., Campbell, J.C. 2013. Factors influencing resource use by African American and African Caribbean women disclosing intimate partner violence. *Journal of Interpersonal Violence*. 28(8):1617–1641. doi: 10.1177/0886260512468326.

266. Ludwig, N.G., Radaeli, R.F., Silva, M.M.X., Romero, C.M., Carrilho, A.J.F., Bessa, D., Macedo, D.B., Oliveira, M.L., et al. 2016. A boy with Prader-Willi syndrome: unmasking precocious puberty during growth hormone replacement therapy. *Archives of Endocrinology and Metabolism*. 60(6):596–600. doi:10.1590/2359-3997000000196.

267. Macey-Dare, L. V. & Goodman, J.R. 1999. Incontinentia pigmenti: seven cases with dental manifestations. *International Journal of Paediatric Dentistry.* 9(4):293–297.

268. Macri, D. V. 2015. stratergies for improving patient compliance. *Dimensions of Dental Hygiene*. 13(12):27–29.

269. Madhoo, S., Kandombo, C., Majozi, N. & Louw, N.E. 2013.Barriers to oral health care in Cape Town. [Unpublished]

270. Magalhães, M.G., Bueno, D.F., Serra, E., Gonçalves, R. 2001. Oral Manifestations of HIV positive children.*Journal of Clinical Pediatric Dentistry*. 25(2):103–106.

271. Mageet, A., 2016. Classification of skeletal and dental malocclusion: revisited. https://doi.org/10.25241/2016.3(2).11

272. Maguire, M. 2009. Anaesthesia for an adult with Angelman syndrome. *Anaesthesia*. 64(11):1250–1253. doi: 10.1111/j.1365-2044.2009.06033. x.

273. Majumdar, U., Arya, G., Singh, S., Pillai, A. & Nair, P.P. 2012. Oro-dental findings in Bardet-Biedl syndrome. *Case Reports*. (apr23 1): bcr1220115320-bcr1220115320. doi:10.1136/bcr.12.2011.5320.

274. Malvania, E., Sheth, S., Sharma, A., Mansuri, S., Shaikh, F., Sahani, S. 2016. Dental caries prevalence among type II diabetic and nondiabetic adults attending a hospital. *Journal of International Society of Preventive and Community Dentistry*. 6(Suppl 3):232-236. doi:10.4103/2231-0762.197202.

275. Mansell, J. 2006. Deinstitutionalisation and community living: progress, problems and priorities. *Journal of Intellectual & Developmental Disability*. 31(2):65–76. doi:10.1080/13668250600686726.

276. Mantadakis, E., Spanaki, A.M., Geromarkaki, E., Vassilaki, E., Briassoulis, G. 2006. Near demise of a child with Prader-Willi syndrome during elective orchidopexy. *Paediatric Anaesthesia*. 16(7):790–793. doi: 10.1111/j.1460-9592.2006.01990. x.

277. Maranhão, M.V.M. 2008. Turner syndrome and anesthesia. *Revista Brasileira de Anestesiologia*. 58(1):84–89.

278. Marca, G. Della, Vasta, I., Scarano, E., Rigante, M., De Feo, E., Mariotti, P., Rubino, M., Vollono, C., et al. 2006. Obstructive sleep apnea in Costello Syndrome. *American Journal of Medical Genetics Part A*. 140(3):257–262. doi:10.1002/ajmg.a.31076.

279. Margari, L., Lamanna, A.L., Buttiglione, M., Craig, F., Petruzzelli, M.G., Terenzio, V. 2013. Long-term follow-up of neurological manifestations in a boy with Incontinentia pigmenti. *European Journal of Pediatrics*. 172(9):1259–1262. doi:10.1007/s00431-013-2021-8.

280. Margolis, S.S., Sell, G.L., Zbinden, M.A., Bird, L.M. 2015. Angelman Syndrome. *Neurotherapeutic.* 12(3):641–650. doi:10.1007/s13311-015-0361-y.

281. Mariño, R.J., Khan, A.R., Tham, R., Khew, C.W.,Stevenson, C. 2014. Pattern and factors associated with utilization of dental services among older adults in rural Victoria. *Australian Dental Journal*. 59(4):504–510. doi: 10.1111/adj.12216.

282. Marques, J.S., Maia, C., Almeida, R., Isidoro, L., Dias, C. 2015. Should patients with Trichorhinophalangeal syndrome be tested for growth hormone deficiency? *Pediatric Endocrinology Reviews*. 13(1):465–467.

283. Marques Pereira, P., Schneider, A., Pannetier, S., Heron, D., Hanauer, A. 2009. Coffin–Lowry syndrome. *European Journal of Human Genetics*. 18(6):627–633. doi:10.1038/ejhg.2009.189.

284. Martelli, H., Paranaíba, L.M.R., de Miranda, R.T., Orsi, J., Coletta, R.D. 2008. Apert syndrome: report of a case with emphasis on craniofacial and genetic features. *Pediatric Dentistry*. 30(6):464–468.

285. Martínez-Macías, F.J., Bobadilla-Morales, L., González-Cruz, J., Quiles-Corona, M., Corona-Rivera, A., Peña-Padilla, C., Orozco-Vela, M., Silva-Cruz, R., et al. 2017. Descriptive Study of the complete blood count in newborn infants with Down syndrome. *American Journal of Medical Genetics Part A.* 173(4):897-904. doi: 10.1002/ajmg.a.38097

286. Martins, R.B., de Souza, R.S. & Giovani, E.M. 2014. Cleidocranial dysplasia: report of six clinical cases. *Special Care in Dentistry*. 34(3):144–150. doi:10.1111/scd.12045.

287. Masamatti, S., Kumar, A. & Virdi, M.S. 2012. Periodontal diseases in children and adolescents: a clinician's perspective part. *Dental Update*. 39(9):639-642.

288. Masiga, M.A. & M'Imunya, J.M. 2013. Prevalence of dental caries and its impact on quality of life (QoL) among HIV-infected children in Kenya. *Journal of Clinical Pediatric Dentistry*. 38(1):83–87.

289. Mass, E., Oelgiesser, D. & Tal, H. 2007. Transitional implants in a patient with Williams-Beuren syndrome: a four-year follow-up. *Special Care in Dentistry.* 27(3):112–116.

290. Matsune, K., Shimizu, T., Tohma, T., Asada, Y., Ohashi, H.,Maeda, T. 2001. Craniofacial and dental characteristics of Kabuki syndrome. *American Journal of Medical Genetics*. 98(2):185–190.

291. Maulik, P., Mascarenhas, M., Mathers, C., Dua, T. and Saxena, S. 2011. Prevalence of intellectual disability: A meta-analysis of population-based studies. *Research in Developmental Disabilities*, 32(2). 419-436.

292. May, P., De Vries, M., Marais, A.S., Kalberg, W., Buckley, D., Adnams, C., Hasken, J., Tabachnick, B., et al. 2017. Replication of high fetal alcohol spectrum disorders prevalence rates, child characteristics, and maternal risk factors in a second sample of rural communities in South Africa. *International Journal of Environmental Research and Public Health*. 14(5):522. doi:10.3390/ijerph14050522.

293. McGovern, E., Owens, L., Nunn, J., Bolas, A., Meara, A.,Fleming, P. 2010. Oral features and dental health in Hurler syndrome following hematopoietic stem cell transplantation *International Journal of Paediatric Dentistry*. 20(5):322–329. doi:10.1111/j.1365-263x.2010.01055. x.

294. McKenna, G., Hayes, M. & Burke, F.M. 2014. Prosthodontic rehabilitation for a patient with acromegaly. *European Journal of Prosthodontics and Restorative Dentistry*. 22(3):98–100.

295. Medeiros, P.J., Camargo, E.S., Vitral, R., Rocha, R. 2000. Orthodontic-surgical approach in a case of severe open-bite associated with functional macroglossia. *American Journal of Orthodontics and Dentofacial Orthopedics.* 118(3):347–351. doi:10.1067/mod.2000.102390.

296. Mellion, Z.J., Behrents,R.G. & Johnston,L.E. 2013. The pattern of facial skeletal growth and its relationship to various common indexes of maturation. *American Journal Orthodontics and Dentofacial Orthopedics.*143(6):845-854. doi: 10.1016/j.ajodo.2013.01.019.

297. Menke, L.A., van Belzen, M.J., Alders, M., Cristofoli, F., Study,D.D., Ehmke, N., Fergelot, P., Foster, A., et al. 2016. *CREBBP* mutations in individuals without Rubinstein-Taybi syndrome phenotype. *American Journal of Medical Genetics. Part A*. 170(10): 2681–2693.doi:10.1002/ajmg.a.37800.

298. Merchant, A.T., 2012. Periodontitis and dental caries occur together. *Journal of Evidence-Based Dental Practice*. 12(s3): 18–19. doi: 10.1016/S1532-3382(12)70005-2

299. Merjaneh, L., Parks, J.S., Muir, A.B., Fadoju, D. 2014. A novel *TRPS1* gene mutation causing Trichorhinophalangeal syndrome with growth hormone responsive short stature: a case report and review of the literature. *International Journal of Pediatric Endocrinology*. 2014(1):16. doi:10.1186/1687-9856-2014-16.

300. Merrick, J., Talnir, R., Gross, S., Chemtob, D., Aspler, S., Kandel, I., Morad, M. 2010. Human Immunodeficiency Virus (HIV) and persons with disability / intellectual disability: a review. *International Public Health Journal*. 2(3):285–288.

301. Mestrovic, S.R., Rajic, Z. & Papic, J.S. 1998. Hypodontia in patients with Down's syndrome. *Collegium Antropologicum.*22 (Suppl):69–72.

302. Meuwissen, M.E.C. & Mancini, G.M.S. 2012. Neurological findings in Incontinentia pigmenti; a review. *European Journal of Medical Genetics*. 55(5):323–331. doi: 10.1016/j.ejmg.2012.04.007.

303. Miller, E., Lee, J.Y., DeWalt, D.A. & Vann, W.F. 2010. Impact of caregiver literacy on children's oral health outcomes. *Pediatrics*. 126(1):107–114. doi: 10.1542/peds.2009-2887.

304. Minde, M. 1975. History of mental health services in South Africa. *South African Medical Journal*. 49(45):1890–1894.

305. Minihan, P.M., Morgan, J.P., Park, A., Yantsides, K.E., Nobles, C.J., Finkelman, M.D., Stark, P.C., Must, A.2014. At-home oral care for adults with developmental disabilities: a survey of caregivers. *Journal of American Dental Association.* 145 (10): 1018–1025.

306. Mixter, R.C., Ewanowski, S.J. & Carson, L. V. 1993. Central tongue reduction for macroglossia. *Plastic and Reconstructive Surgery*. 91(6):1159–1162.
307. Mohan, S. 2016. Prime drug interplay in dental practice. *Journal of Clinical and Diagnostic Research*. 10(3): ZE07–ZE11. doi:10.7860/jcdr/2016/16912.7434.
308. Molteno, C., Smart, R., Viljoen, D., Sayed, R.,Roux, A. 1997. Twenty-year birth prevalence of Down syndrome in Cape Town, South Africa. *Paediatric and Perinatal Epidemiology*. 11(4):428–435.
309. Monfared, A. & Messner, A. 2006. Death following tonsillectomy in a child with Williams syndrome. *International Journal of Pediatric Otorhinolaryngology*. 70(6):1133–1135. doi: 10.1016/j.ijporl.2005.11.009.
310. Morgan, J. 2007. Why is periodontal disease more prevalent and more severe in people with Down syndrome? *Special Care in Dentistry*. 27(5):196–201. doi: 10.1111/j.1754-4505. 2007.tb00346. x.
311. Morgan, J.P., Minihan, P.M., Stark, P.C., Finkelman, M.D., Yantsides, K.E., Park, A., Nobles, C.J., Tao, W. & et al. 2012. The oral health status of 4,732 adults with intellectual and developmental disabilities. *Journal of the American Dental Association*. 143(8):838–846.
312. Morita, Y., Kimoto, N., Ogawa, H., Omata, T., Morita, N. 2011. Simpson-Golabi-Behmel syndrome associated with cleft Palate. *Journal of Craniofacial Surgery*. 22(5):1917–1918. doi: 10.1097/SCS.0b013e31822ea73c.
313. Moskovitz, M., Brener, D., Faibis, S., Peretz, B. 2005. Medical considerations in dental treatment of children with Williams syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 99(5):573–580.doi: 10.1016/j.tripleo.2004.03.019
314. Motzkin, N.E., Bianco, A.J. & Zimmerman, D. 1992. Tibia vara in a patient with Bardet-Biedl syndrome. *Mayo Clinic Proceedings*. 67(6):549–552.
315. Moura, C.P., Cunha, L.M., Vilarinho, H., Cunha, M.J., Freitas, D., Palha, M., Pueschel, S.M., Pais-Clemente, M. 2008. Voice parameters in children with Down syndrome. *Journal of Voice.* 22(1):34–42. doi: 10.1016/j.jvoice.2006.08.011.
316. Mouradian, W.E. 2001. The face of a child: children's oral health and dental education. *Journal of Dental Education*. 65(9):821–831. doi: 10.1177/001789690106000411.
317. Murakami, C., Nahas Pires Correa, M.S., Nahas Pires Correa, F., Nahas Pires Correa, J.P. 2008. Dental treatment of children with Angelman syndrome: a case report. *Special Care in Dentistry.* 28(1):8–11. doi:10.1111/j.1754-4505.2008.00003. x.
318. Nagori, S.A., Jose, A., Agarwal, B., Bhatt, K., Bhutia, O., Roychoudhury, A. 2014. Traumatic bone cyst of the mandible in Langer-Giedion syndrome: a case report. *Journal of Medical Case Reports*. 8:387. doi:10.1186/1752-1947-8-387.
319. Naidoo, S. & Chikte, U. 2004. Oro-facial Manifestations in paediatric HIV: a comparative study of institutionalized and hospital outpatients. *Oral Diseases*. 10(1):13–18. doi:10.1046/j.1354-523x.2003.00973. x.

320. Nakayama, M., Lähdesmäki, R., Niinimaa, A., Alvesalo, L. 2015. Molar morphology and the expression of carabelli's trait in 45X females. *American Journal of Human Biology*. 27(4):486–493. doi:10.1002/ajhb.22674.

321. Nargozian, C. 2004. The airway in patients with craniofacial abnormalities. *Paediatric Anaesthesia*. 14:53–59. doi:10.1046/j.1460-9592.2003.01200. x.

322. Nathan, J.E. 2001. Behavioral management strategies for young pediatric dental patients with disabilities. *ASDC Journal of Dentistry for Children*. 68(2):89–101.

323. Needham, M., Packman, W., Rappoport, M., Quinn, N., Cordova, M., Macias, S., Morgan, C., Packman, S. 2014. MPS II: adaptive behavior of patients and impact on the family system. *Journal of Genetic Counseling*. 23(3):330–338. doi:10.1007/s10897-013-9665-4.

324. Needham, M., Packman, W., Quinn, N., Rappoport, M., Aoki, C., Bostrom, A., Cordova, M., Macias, S., et al. 2015. Health-related quality of life in patients with MPS II. *Journal of Genetic Counseling*. 24(4):635–344. doi:10.1007/s10897-014-9791-7.

325. Neely, J., Carpenter, J., Hsu, W., Jordan, L., Restrepo, L. 2006. Cerebral infarction in Hunter syndrome. *Journal of Clinical Neuroscience.* 13(10):1054–1057. doi: 10.1016/j.jocn.2005.12.038.

326. Nemutandani, M.S., Adedoja, D. & Nevhuhlwi, D. 2013. Dental caries among disabled individuals attending special schools in Vhembe district. South Africa..*South African Dental Journal.*68(10):458–461.

327. Nibali, L., Di Iorio, A., Tu, Y.K., Vieira, A.R., 2017. Host genetics role in the pathogenesis of periodontal disease and caries. *Journal of Clinical. Periodontology*. 44 Suppl 18, S52–S78. doi.org/10.1111/jcpe.12639

328. Nicita, F., Ruggieri, M., Polizzi, A., Mauceri, L., Salpietro, V., Briuglia, S., Papetti, L., Ursitti, F., et al. 2012. Seizures and epilepsy in Sotos syndrome: analysis of 19 caucasian patients with long-term follow-up. *Epilepsia*. 53(6): e102-e105. doi:10.1111/j.1528-1167.2012.03418. x.

329. Nirje, B. 1994. The normalization principle and its human management implications. *International Social Role Valorization Journal*. 1(2):19–23.

330. Nishimoto, H.K.,Jones, J.R., Dwivedi, A., Cho, H.M., Layman, L.C., Kim, H.G. 2014. The historical Coffin-Lowry syndrome family revisited: identification of two novel mutations of *RPS6KA3* in three male patients. *American Journal of Medical Genetics.Part A*. 16(9):2172–2179. doi:10.1002/ajmg.a.36488.

331. Njenga, F. 2009. Perspectives of intellectual disability in Africa: epidemiology and policy services for children and adults. *Current Opinion in Psychiatry*. 22(5):475–461.

332. Nobbs, A. 2016. Getting to the heart of the matter: role of *Streptococcus Mutans Adhesin Cnm* in systemic disease.*Virulence*. 8(1):1-4. doi:10.1080/21505594.2016.1212157.

333. Nobili, V., Marcellini, M., Devito, R., Capolino, R., Viola, L. Digilio, M.C. 2004. Hepatic fibrosis in Kabuki syndrome. *American Journal of Medical Genetics. Part A*. 124(2):209–212. doi:10.1002/ajmg.a.20387.

334. Norderyd, J. & Aronsson, J. 2012. Hypoplastic root cementum and premature loss of primary teeth in Coffin-Lowry syndrome: a case report. *International Journal of Paediatric Dentistry.* 22(2):154–156. doi:10.1111/j.1365-263x.2011.01160. x.

335. Norwood, K.W. & Slayton, R.L. 2013. Oral health care for children with developmental disabilities. *American Academy of Pediatrics*.131(3):614–619. doi: 10.1542/peds.2012-3650.
336. Novotna, M., Podzimek, S., Broukal, Z., Lencova, E., Duskova, J. 2015.Periodontal diseases and dental caries in children with type 1 Diabetes Mellitus. *Mediators of Inflammation*. 2015:1-8. doi:10.1155/2015/379626.
337. Nqcobo, C., Yengopal, V. & Rudolf, M. 2012. Caries prevalence of children attending special needs schools in Johannesburg, Gauteng, South Africa. *South African Dental Journal*. 67(7):308–313.
338. Nyland, E. 2002. *The Maleus Malificorum: Summation of the Maleus Malificarum*. Available: http://www.bibliotecapleyades.net/cienciareal/cienciareal12.htm [2016, January 19].
339. O'Neil, D.W., Canada, R.T., Clark, M. V., Lowe, J.W. 1989. Rubinstein-Taybi syndrome: case report. *Pediatric Dentistry*. 11(2):158–160.
340. Oghan, F., Harputluoglu, U., Guclu, E., Guvey, A., Turan, N., Ozturk, O. 2007. Permanent T-tube insertion in two patients with Hurler's syndrome. *International Journal of Audiology*. 46(2):94–96. doi:10.1080/14992020600975287.
341. Ohshita, N., Tomiyama, Y., Iseki, A., Kawano, H., Kakuta, N., Tsutsumi, Y.M., Oshita, S.P. 2010. Anesthetic management of a child with Angelman's syndrome [Abstract]. *Masui.* 59(4):484–486.
342. Olczak-Kowalczyk, D., Witt, A., Gozdowski, D., Ginalska-Malinowska, M. 2011. Oral mucosa in children with Prader-Willi syndrome. *Journal of Oral Pathology and Medicine*. 40(10):778–784. doi:10.1111/j.1600-0714.2011.01034. x.
343. Opal, S., Garg, S., Jain, J. & Walia, I. 2015. Genetic factors affecting dental caries risk. *Australian Dental Journal*, 60(1):2-11.
344. Oredugba, F.A. & Akindayomi, Y. 2008. Oral health status and treatment needs of children and young adults attending a day centre for individuals with special health care needs.*BMC Oral Health*. 8:30. doi:10.1186/1472-6831-8-30.
345. Oyedeji, O.A., Gbolahan, O.O., Oluwatoyin Abe, E., Agelebe, E. 2015. Oral and dental lesions in HIV infected Nigerian children. *Pan African Medical Journal*. 20:287. doi:10.11604/pamj.2015.20.287.5273.
346. Ozer, G., Yüksel, B., Süleymanova, D., Alhan, E., Demircan, N., Onenli, N. 1995. Clinical features of Bardet-Biedl syndrome. *Acta Paediatrica Japonica.*37(2):233–236.
347. Paludetti, G., Zampino, G., Della Marca, G., Di Girolamo, S., Scarano, E., Rigante, M. 2003. The tongue-base suspension using repose bone screw system in a child with Simpson-Golabi-Behmel syndrome. Case Report. *International Journal of Pediatric Otorhinolaryngology*. 67(10):1143–1147. doi:10.1016/s0165-5876(03)00220-9.
348. Paradowska-Stolarz, A.M. 2014. Wolf-Hirschhorn syndrome (WHS) - literature review on the features of the syndrome. *Advances in Clinical and Experimental Medicine*. 23(3):485–489.
349. Parini, R., Jones, S.A., Harmatz, P.R., Giugliani, R. M.N. 2016. The natural history of growth in patients with Hunter syndrome: data from the Hunter Outcome Survey (HOS). *Molecular Genetic Metabolsim.* 117(4):438–46. doi: 10.1016/j.ymgme.2016.01.009.

350. Park, C.H., Park, K.H. & Choi, B.Y. 2012. Management of anesthesia for Rubinstein-Taybi syndrome. *Korean Journal of Anesthesiology*. 63(6):571–572. doi: 10.4097/kjae.2012.63.6.571.

351. Patel, K., Chavan, D. & Sawant, P. 2013. Anesthesia management in a patient of Apert syndrome. *Anesthesia, Essays and Researches*. 7(1):133–135. doi: 10.4103/0259-1162.114021.

352. Patel, V., Simbine, A.P.F., Soares, I.C., Weiss, H.A.,Wheeler, E. 2007. Prevalence of severe mental and neurological disorders in Mozambique: a population-based survey. *Lancet*. 370(9592):1055–1060.

353. Pavone, M., Caldarelli, V., Khirani, S., Colella, M., Ramirez, A., Aubertin, G., Crinò, A., Brioude, F., et al.2015. S. Disordered breathing in patients with Prader-Willi. syndrome: a. multicenter study. *Pediatric Pulmonology*. 50(12):1354–1359. doi:10.1002/ppul.23177.

354. Peacock, M.E., Arce, R.M. & Cutler, C.W. 2017. Periodontal and other oral manifestations of immunodeficiency diseases. *Oral Diseases*.23(7):866-888. doi:10.1111/odi.12584.

355. Pentinpuro, R.H., Lähdesmäki, R.E. & Alvesalo, L.J. 2013. Root lengths in the permanent teeth of 45X females. *Acta Odontologica Scandinavica*. 71(3–4):778–785. doi:10.3109/00016357.2012.734399.

356. Pentinpuro, R.H., Lähdesmäki, R.E., Niinimaa, A.O., Pesonen, P.R.O., Alvesalo, L.J. 2014. Crown heights in the permanent teeth of 45X and 45X/46XX females. *Acta Odontologica Scandinavica*. 72(8):908–916. doi:10.3109/00016357.2014.921327.

357. Pereyra, M., Metsch, L.R., Tomar, S., Valverde, E., Jeanty, Y., Messinger, S., Boza, H. 2011. Utilization of dental care services among low-income HIV-positive persons receiving primary care in South Florida. *AIDS Care*.23(1):98–106.doi: 10.1080/09540121.2010.498861.

358. Perillo, L., Monsurrò, A., Bonci, E., Torella, A., Mutarelli, M., Nigro, V. 2015. Genetic association of *ARHGAP21* gene variant with mandibular prognathism. *Journal of Dental Research*. 94(4):569–576. doi: 10.1177/0022034515572190.

359. Petersen, I., Bhana, A., Campbell-Hall, V., Mjadu, S., Lund, C., Kleintjies, S., Hosegood, V., Flisher, A.J., et al. 2009. Planning for district mental health services in South Africa: a situational analysis of a rural district site. *Health Policy and Planning*. 24(2):140–150. doi:10.1093/heapol/czn049.

360. Petrovic, B.B., Peric, T.O., Markovic, D.L.J., Bajkin, B.B., Petrovic, D., Blagojevic, D.B., Vujkov, S. 2016. Unmet oral health needs among persons with intellectual disability. *Research in Developmental Disabilities*. 59:370–377. doi: 10.1016/j.ridd.2016.09.020.

361. Petković, G. & Barišić, I. 2013. Prevalence of fetal alcohol syndrome and maternal characteristics in a sample of schoolchildren from a rural province of Croatia. *International Journal of Environmental Research and Public Health*. 10(4):1547–1561. doi:10.3390/ijerph10041547.

362. Petzold, D., Kratzsch, E., Opitz, C.,Tinschert, S. 2003. The Kabuki syndrome: four patients with oral abnormalities. *European Journal of Orthodontics*. 25(1):13–19.

363. Picksak, G., Höner zu Siederdissen, C. & Stichtenoth, D.O. 2010. SSRI-associated bleeding risk. [Abstract]. *Medizinische Monatsschrift Fur Pharmazeuten*. 33:217–218.

364. Pizzamiglio, M.R., Piccardi, L., Bianchini, F., Canzano, L., Palermo, L., Fusco, F., D'Antuono, G., Gelmini, C., et al. 2014. Incontinentia pigmenti: learning disabilities are a fundamental hallmark of the disease. *PLoS ONE*. 9(1). doi: 10.1371/journal.pone.0087771. Availabe at: https://doi.org/10.1371/journal.pone.0087771 doi: 10.1371/journal.pone.0087771

365. Prosman, G.J., Lo Fo Wong, S.H., Lagro-Janssen, A.L.M. 2014. Why abused women do not seek professional help: a qualitative study. *Scandinavian Journal of Caring Sciences*. 28(1):3–11. doi: 10.1111/scs.12025.

366. Puri, S., Bhattarai, D., Adhikari, P., Shrestha, J.B., Paudel, N. 2015. Burden of ocular and visual disorders among pupils in special schools in Nepal. *Archives of Disease in Childhood*. 100(9):834–837. doi:10.1136/archdischild-2014-308131.

367. Purohit, B.M., Acharya, S. & Bhat, M. 2010. Oral health status and treatment needs of children attending special schools in south India: a comparative study. *Special Care in Dentistry*. 30:235–241.

368. Ram, G. & Chinen, J. 2011. Infections and immunodeficiency in Down syndrome. *Clinical and Experimental Immunology*. 164(1):9–16. doi: 10.1111/j.1365-2249.2011.04335. x.

369. Ramachandra, S., Singh, A. & Wong, D. 2015. Dental management of patient with Williams syndrome - a case Report. *Contemporary Clinical Dentistry*. 6(3):418-420. doi:10.4103/0976-237x.161908

370. Ramalingam, K., Kaliyamurthy, S., Govindarajan, M., Swathi, S. 2012. Seckel syndrome: a report of a case. *Journal of Indian Society of Pedodontics and Preventive Dentistry*. 30(3):258-261. doi:10.4103/0970-4388.105021.

371. Ravindran, O.S., Rani, M.P. & Priya, G. 2014. Cognitive deficits in HIV infected children. *Indian Journal of Psychological Medicine*. 36(3):255–259. doi:10.4103/0253-7176.135373.

372. Reed, A., Thomas, J., Roelofse, J., Gray, R. 2010. Guidelines for the safe use of procedural sedation and analgesia for diagnostic and therapeutic procedures in children. *South African Journal of Anesthesia and Analgesia*. 16(5):S1–S37.

373. Regen, A., Nelson, L.P. & Woo, S.B. 2010. Dental manifestations associated with Seckel syndrome type II: a case report. *Pediatric Dentistry*. 32(5):445–450.

374. Reid, B.C., Chenette, R. & Macek, M.D. 2012. Special Olympics: the oral health status of U.S. athletes compared with international athletes. *Special Care in Dentistry.* 23(6):230–233.

375. Rendall-Mkosi, K., London, L., Adnams, C., Morojele, N., McLoughlin, J. A.,Goldstone, C. 2008. Fetal alcohol spectrum disorder in South Africa: situational and gap analysis. *Medical Research Council*. [Available at: https://www.unicef.org/southafrica/SAF_resources_fetalalcohol.pdf]

376. Reynalds, T., Zupanick, C. & Dombeck, K. 2015. *Early Medical Explanations of Intellectual Disability*. Available: https://www. mentalhelp.net/articles/early-medical-explanations-of-intellectual-disability/ [2016, January 20].

377. Ribeiro, E.M., Fonteles, C.S.R., Freitas, A.B., da Silva Alves, K.S., Monteiro, A.J., da Silva, C.A.B. 2014. A clinical multicenter study of orofacial features in 26 Brazilian patients with different types of mucopolysaccharidosis. *The Cleft Palate-Craniofacial Journal.* 52(3):352–358. doi:10.1597/13-204.

378. Riise, R., Andréasson, S., Borgaström, M.K., Wright, A.F., Tommerup, N., Rosenberg, T., Tornqvist, K. 1997. Intrafamilial variation of the phenotype in Bardet-Biedl syndrome. *British Journal of Ophthalmology*. 81(5):378–385.

379. Roberts, T., Stephen, L.X.G., Fieggen, K., Beighton, P. 2009. Wolf-Hirschhorn syndrome; oro-dental manifestations and management. *Journal of Clinical Pediatric Dentistry*. 34(2):173–176.

380. Roberts, T., Stephen, L., & Beighton, P., 2013. Cleidocranial dysplasia: a review of the dental, historical, and practical implications with an overview of the South African experience. *Oral Surgery. Oral Medicine Oral Pathology. Oral Radiology.* 115(1): 46–55.doi.10.1016/j.oooo.2012.07.435

381. Roeleveld, N. and Zielhuis, G. 2008. The prevalence of mental retardation: a critical review of recent literature. *Developmental Medicine & Child Neurology*, 39(2):125-132.

382. Ropers, H.H.2010. Genetics of early onset cognitive impairment. *Annual Review of Genomics and Human Genetics*. 11:161-187. doi: 10.1146/annurev-genom-082509-141640

383. Rosanowski, F., Hoppe, U., Proschel, U., Eysholdt, U. 1998. Late-onset sensorineural hearing loss in Coffin-Lowry syndrome. *Journal for Oto-Rhino-Laryngology and Its Related Specialties*. 60(4):224–226.

384. Rushton, P. 1988. Lunatics and idiots: mental disability, the community, and the poor law in North-East England,1660-1800. *Medical History*. 32(1):34–50.

385. Rwenyonyi, C.M., Kutesa, A., Muwazi, L., Okullo, I., Kasangaki, A., Kekitinwa, A. 2011. Oral manifestations in HIV/AIDS-infected children. *European Journal of Dentistry*. 5(3):291–298.

386. Sá-Pinto, A.C., Rego, T.M., Marques, L.S., Martins, C.C., Ramos-Jorge, M.L., Ramos-Jorge, J. 2018. Association between malocclusion and dental caries in adolescents: a systematic review and meta-analysis. *European Archives of Paediatric Dentistry*. 19(2): 73–82.

387. Saeves, R., Nordgarden, H., Storhaug, K., Sandvik, L., Espelid, I. 2012. Salivary flow rate and oral findings in Prader-Willi syndrome: a case-control Study. *International Journal of Paediatric Dentistry*. 22(1):27–36. doi:10.1111/j.1365-263x.2011.01153. x.

388. Sarkar, P.A., Shigli, A. & Patidar, C. 2011. Happy Puppet syndrome. *BMJ Case Reports*. 2011. 2011: bcr0920114747. doi:10.1136/bcr.09.2011.4747.

389. Sales-peres, S.H.D.C. 2012. Oral manifestations in HIV + children in Mozambique. *Ciencia & Saude Coletiva*. 17(1):55–60. doi:10.1590/s1413-81232012000100008.

390. Sammon, M.R., Doyle, D., Hopkins, E., Sol-Church, K., Stabley, D.L., McGready, J., Schulze, K., Alade, Y., et al. 2012. Normative growth charts for individuals with Costello syndrome. *American Journal of Medical Genetics. Part A*. 158(11):2692–2699. doi:10.1002/ajmg.a.35534.

391. SAPS. 2016. Crime situation in South Africa April 2015 -March 2016. Available: http://www.saps.gov.za/services/final-crime-stats-release-02september2016.pdf.

392. Sarkar, P.A., Shigli, A. & Patidar, C. 2011. Happy Puppet syndrome. *BMJ Case Reports*. 2011. doi:10.1136/bcr.09.2011.4747.

393. Sattur, A., Deshmukh, P.K., Abrahim, L., Naikmasur, V.G. 2014. Kabuki Make-up syndrome - a case report with electromyographic study. *Journal of Clinical and Diagnostic Research.* 8(11):ZD03-6. doi:10.7860/jcdr/2014/9804.5122.

394. Saunders, M., Lewis, P. & Thornhill, A., 2015. *Research Methods for Business Students.* 6th Ed. London, UK: Pearson.

395. Sauer, C., Schlüter, B., Hinz, R., Gesch, D. 2012. Childhood obstructive sleep apnea syndrome: an interdisciplinary approach: a prospective epidemiological study of 4,318 five-and-a-half-year-old children. *Journal of Orofacial Orthopedics*. 73(5): 342–358. doi:10.1007/s00056-012-0096-x

396. Saurabh, G., Krishnamoorthy, S., Nandan, S., Ambili, A., Savitha, N. 2015. Hunter's Syndrome: a case report. *Journal of Indian Society of Pedodontics and Preventive Dentistry*.33(1): 66.doi:10.4103/0970-4388.149011.

397. Savitha, N.S., Saurabh, G., Krishnamoorthy, S.H., Nandan, S. & Ambili, A. 2015. Hunter's syndrome: a case report. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 33(1):66–68. doi:10.4103/0970-4388.149011

398. Scardina, G., Fuca, G. & Messina, P. 2007. Oral diseases in a patient affected with Prader-Willi syndrome. *European Journal of Paediatric Dentistry.*8(2):96–99.

399. Schneider, M., Claasens, M., Kimmie, Z., Morgan, R., Naicker, S., Roberts, A., McLarenet, P. 1999. *The extent of moderate and severe reported disability and nature of the disability experience in South Africa.* Commissioned by the Department of Health, Pretoria. Conducted by the Community Agency for Social Enquiry (CASE).

400. Scrimshaw, N.S., Taylor, C.E. & Gordon, J.E., 1968. Interactions of nutrition and infection. *Monograph Series. World Health Organization.* 57: 3–329.

401. Seidman, L.J., Buka, S.L., Goldstein, J.M., Horton, N.J., Rieder, R.O., Tsuang, M.T. 2000. The relationship of prenatal and perinatal complications to cognitive functioning at age 7 in the new england cohorts of the national collaborative perinatal project. *Schizophrenia Bulletin*. 26(2):309–321.

402. Serrera Figallo, M., Velázquez Cayón, R., Lagares, D.T., Corcuera Flores, J.R., Portillo, G.M. 2012.Use of anesthetics associated to vasoconstrictors for dentistry in patients with cardiopathies. *Journal of Clinical and Experimental Dentistry*. 4(2):107–111.doi:10.4317/jced.50590.

403. Seymen, F., Tuna, B. & Kayserili, H. 2002. Seckel syndrome: report of a case. *Journal of Clinical Pediatric Dentistry*. 26(3):305–309.

404. Shafer, W.G., Hine, M.K., & Levy, B.M. 1983. Develpmental Disturbances of oral and paraoral structures. In *A Textbook of Oral Pathology*.4th ed. Philadelphia: W. B. Saunders Co. p37.

405. Shapira, Y., Lubit, E., & Kuftinec, M.M.1999. Congenitally missing second premolars in cleft lip and cleft palate children. *American Journal of Orthodontics and Dentofacial Orthopedics.* 115(4):396-400.

406. Sher, A.E. 1992. Mechanisms of Airway obstruction in Robin sequence: implications for treatment. *Cleft Palate-Craniofacial Journal*. 29(3):224–231. doi: 10.1597/1545-1569(1992)029<0224:MOAOIR>2.3.CO;2.

407. Shereenberger, RC. A history of mental retardation. Baltimore: Brookes Publishing Co. 1983
408. Sherr, L., Mueller, J. & Varrall, R. 2009. A systematic review of cognitive development and child human immunodeficiency virus infection. *Psychology, Health & Medicine*. 14(4):387–404. doi:10.1080/13548500903012897.
409. Shivakumar, K., Patil, S., Kadashetti, V., Raje, V. 2018. Oral Health Status and Dental Treatment Needs of 5–12-year-old Children with Disabilities Attending Special Schools in Western Maharashtra, India. *International Journal of Applied and Basic Medical Research.* 81): 24–29. doi: 10.4103/ijabmr.IJABMR_57_17
410. Silveira, M.L., Whitcomb, B.W., Pekow, P., Carbone, E.T., Chasan-Taber, L. 2016. Anxiety, depression, and oral health among US pregnant women: behavioral risk factor surveillance system. *Journal of Public Health Dentistry*. 76(1):56–64.doi: 10.1111/jphd.12112.
411. Simmons, H.C., Oxford, D.E., Hill, M.D. 2008. The prevalence of skeletal Class II patients found in a consecutive population presenting for TMD treatment compared to the national average. *The Journal of the Tennessee Dental Association*. 88 (4): 16–18.
412. Singh, A., Bhatia, H.P. & Sharma, N. 2017. Coexistence of fusion and concrescence of primary teeth: in a child with Down syndrome. *Special Care in Dentistry*. 37(3):147–149.doi:10.1111/scd.12218.
413. Singh, P. 2013. Systemic toxicity of local anesthetics: a point to ponder. *Toxicology Internationl.*20(2):194. doi: 10.4103/0971-6580.117273ompson
414. Sinha, R., Thangaswamy, C.R., Muthiah, T., Chandra, P., Subramaniam, R. 2011. Prolonged postoperative desaturation in a child with Down syndrome and atrial septal defect. *Indian Journal of Anaesthesia*. 55(6):608–610. doi: 10.4103/0019-5049.90619.
415. Sirmaci, A., Spiliopoulos, M., Brancati, F., Powell, E., Duman, D., Abrams, A., Bademci, G., Agolini, E. et al. 2011. Mutations in *ANKRD11* cause KBG syndrome, characterized by intellectual disability, skeletal malformations, and macrodontia. *American Journal of Human Genetics*. 89(2):289–294. doi: 10.1016/j.ajhg.2011.06.007.
416. Slade, G.D., Nuttall, N., Sanders, A.E., Steele, J.G., Allen, P.F., Lahti, S. 2005. Impacts of oral disorders in the United Kingdom and Australia. *British Dental Journal*. 198(8):489–493. doi: 10.1038/sj.bdj.4812252.
417. Slayton, R. 2006. Genetics and environmental factors play important roles in the risk for periodontal disease and edentulism. *Journal of Evidence Based Dental Practice*, 6(3):238-239.
418. Smit, D.A., Barrie, R.B. & Louw, A.J. 2017. The burden of dental caries in the Western Cape and a recommended turn-around strategy. *South African Dental Journal.* 72(8):360–365.
419. Smith, C.B. & Waite, P.D. 2012. Surgical management of obstructive sleep apnea in acromegaly with mandibular prognathism and macroglossia: a treatment dilemma. *Journal of Oral and Maxillofacial Surgery.* 70(1):207–210. doi: 10.1016/j.joms.2011.05.022.

420. Soancă, A., Dudea, D., Gocan, H., Roman, A., Culic, B. 2010. Oral manifestations in Apert syndrome: case presentation and a brief review of the literature. *Romanian Journal of Morphology and Embryology.* 51(3):581–584. doi: 510310581584.

421. Sobral, S.D.P., Leite, A.F., Figueiredo, P.T.S., Ferrari, I., Safatle, H.P.N., Cordoba, M.S., Versiani, B.R., Acevedo, A.C., et al. 2013. Craniofacial and dental features in Kabuki syndrome patients.. *Cleft Palate-Craniofacial Journal*. 50(4):440–447. doi:10.1597/11-052.

422. Soylu, N., Alpaslan, A.H., Ayaz, M., Esenyel, S., Oruç, M. 2013. Psychiatric disorders and characteristics of abuse in sexually abused children and adolescents with and without intellectual disabilities. *Research in Developmental Disabilities*. 34(12):4334–4342. doi: 10.1016/j.ridd.2013.09.010.

423. Spano, G., Campus, G., Bortone, A., Lai, V., Lugliè, P.F. 2008. Oral features in Kabuki make-up syndrome. *European Journal of Paediatric Dentistry.* 9(3):149–152.

424. Stanley, B.O.C., Feingold, E., Cooper, M., Vanyukov, M.M., Maher, B.S., Slayton, R.L., Willing, M.C., Reis, S.E., & et al. 2014. Genetic Association of MPPED2 and ACTN2 with Dental Caries. *Journal of Dental. Research*. 93, 626–632. doi.org/10.1177/0022034514534688.

425. Starbuck, J., Reeves, R.H. & Richtsmeier, J. 2011. Morphological integration of soft-tissue facial morphology in Down syndrome and siblings. *American Journal of Physical Anthropology*. 146(4):560–568. doi:10.1002/ajpa.21583.

426. Statistics South Africa.2005. CENSUS 2001-Prevalence of disability in South Africa. Available at: http://bethesdahoutbay.co.za/documents/CENSUS%202001%20REPORT.Disabilities%20in%20South%20Africa.pdf

427. Statistics South Africa. 2007. *Statistical Community Survey , 2007 (Revised Version)*. Available at: https://www.statssa.gov.za/publications/P0301/P0301.pdf

428. Statistics South Africa. 2014. *Census 2011: Profile of persons with disabilities in South Africa.* Available at:. http://www.statssa.gov.za/publications/Report-03-01-59/Report-03-01-592011.pdf

429. Statistics South Africa. 2016. *Work and Labour Force: South Africa*. Available: http://www.statssa.gov.za/?cat=31 [2017, March 08].

430. Stiles,K. A. & Luke,J.E. 1953. The inheritance of malocclusion due to mandibular prognathism. *Journal of Hereditary.* 44:241–245.

431. Subasioglu, A., Savas, S., Kucukyilmaz, E., Kesim, S., Yagci, A. & Dundar, M. 2015. Genetic background of supernumerary teeth. *European Journal of Dentistry*. 9(1):153–158. doi:10.4103/1305-7456.149670.

432. Subbiah, S., Chinnathurai, R., Sangumani, J., Somasundaram, S. 2016. A rare association of obesity, diabetes mellitus and bilateral cryptorchidism: Prader - Willi syndrome. *Journal of the Association of Physicians of India*. 64(11):97–98.

433. Subramaniam, D.R., Mylavarapu, G., McConnell, K., Fleck, R.J., Shott, S.R., Amin, R.S., Gutmark, E.J. 2016. Upper airway elasticity estimation in pediatric Down syndrome sleep apnea patients using collapsible tube theory. *Annals of Biomedical Engineering*. 44(5):1538–1552. doi:10.1007/s10439-015-1430-4.

434. Suprabha, B.S., Rao, A., Choudhary, S., Shenoy, R. 2011. Child dental fear and behavior: the role of environmental factors in a hospital cohort. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 29(2):95–101. doi:10.4103/0970-4388.84679.

435. Suri, S., Tompson, B.D. & Cornfoot, L. 2010. Cranial base, maxillary and mandibular morphology in Down syndrome. *Angle Orthodontist*. 80(5):861–869. doi: 10.2319/111709-650.1.

436. Suri, S., Tompson, B.D. & Atenafu, E. 2011. Prevalence and patterns of permanent tooth agenesis in Down syndrome and their association with craniofacial morphology. *Angle Orthodontist*. 81(2):260–269. doi:10.2319/070910-391.1.

437. Suspitsin, E.N. & Imyanitov, E.N. 2016. Bardet-Biedl Syndrome. *Molecular Syndromology*. 7(2):62–71.doi:10.1159/000445491.

438. Suzuki, K., Muramatsu, H., Okuno, Y., Narita, A., Hama, A., Takahashi, Y., Yoshida, M., Horikoshi, Y., et al. 2016. Immunosuppressive therapy for patients with Down syndrome and idiopathic aplastic anemia. *International Journal of Hematology*. 104(1):130–133. doi:10.1007/s12185-016-1997-z.

439. Taggart, L., Coates, V. & Truesdale-Kennedy, M. 2013. Management and quality indicators of Diabetes Mellitus in people with intellectual disabilities. *Journal of Intellectual Disability Research.*57(12):1152–1163. doi:10.1111/j.1365-2788.2012.01633. x.

440. Takahashi, M. & Ohashi, H. 2013. Craniofacial and dental malformations in Costello syndrome: A detailed evaluation using multi-detector row computed tomography. *Congenital Anomalies*. 53(2):67–72. doi:10.1111/cga.12004.

441. Tamazawa, Y., Watanabe, M., Kikuchi, M., Takatsu, M., Tamazawa, K., Yumoto, N., Hyvarinen, P. 2004. A new dental unit for both patients in wheelchairs and general patients. *Gerodontology*. 21(1):53–59.

442. Tannure, P.N., Oliveira, C.A.G.R., Maia, L.C., Vieira, A.R., Granjeiro, J.M., Costa, M. 2012. Prevalence of dental anomalies in nonsyndromic individuals with cleft lip and palate: a systematic review and meta-analysis. *Cleft Palate-Craniofacial Journal.* 49(2):194–200. doi: 10.1597/10-043.

443. Tasioula, V., Balmer, R. & Parsons, J.2008.Dental health and treatment in a group of children with congenital heart disease. *Pediatric Dentistry*. 30(4):323–328.

444. Tassé, M.J., Luckasson, R. & Nygren, M. 2013. AAIDD proposed recommendations for *ICD–11* and the condition previously known as mental retardation. *Intellectual and Developmental Disabilities*. 51(2):127–131. doi:10.1352/1934-9556-51.2.127.

445. Taylor, G.W. & Borgnakke, W.S. 2008.Periodontal disease: associations with diabetes, glycemic control and complications.*Oral Diseases*.14(3):191–203. doi:10.1111/j.1601-0825.2008.01442. x.

446. Tecco, S., Crincoli, V., Di Bisceglie, B., Saccucci, M., MacrÍ, M., Polimeni, A., Festa, F. 2011. Signs and symptoms of temporomandibular joint disorders in caucasian children and adolescents. *Cranio.* 29(1):71–79. doi: 10.1179/crn.2011.010.

447. Teixeira, C.S., Silva, C.R., Honjo, R.S., Bertola, D.R., Albano, L.M., Kim, C.A. 2009. Dental evaluation of Kabuki syndrome patients. *Cleft Palate-Craniofacial Journal*. 46(6):668–673. doi:10.1597/08-077.1

448. Tekin M, Fitoz S, Arici S, Cetinkaya E, I.A. 2006. Niikawa-Kuroki (Kabuki) syndrome with congenital sensorineural deafness: evidence for a wide spectrum of inner ear abnormalities. *International Journal of Pediatriac Otorhinolaryngology.* 70(5):885–889. doi: 10.1016/j.ijporl.2005.09.025.

449. Thakur, A.R., Naikmasur, V.G. & Sattur, A. 2015. Hurler syndrome: orofacial, dental, and skeletal findings of a case. *Skeletal Radiology*. 44(4):579–586. doi:10.1007/s00256-014-1982-7.

450. Thomas, S. & Tandon, S. 2000. Hurler syndrome: a case report. *The Journal of Clinical Pediatric Dentistry*. 24(4):335–338.

451. Tlhabye, G. (2018). Life Esidimeni mental patients died of hunger, cold | IOL News. [online] Iol.co.za. Available at: https://www.iol.co.za/news/south-africa/gauteng/life-esidimeni-mental-patients-died-of-hunger-cold-7591663.

452. Topouzelis, N.,Iliopoulos, C. & Kolokitha, O. 2011.Macroglossia. *International Dental Journal.*61(2):63-69

453. Torres, C.P., Valadares, G., Martins, M.I., Borsatto, M.C., Díaz-Serrano, K.V.,de Queiroz, A.M. 2015. Oral findings and dental treatment in a child with Williams-Beuren syndrome. *Brazilian Dental Journal*. 26(3):312–316. doi:10.1590/0103-6440201300335.

454. Trihandini, I., Wiradidjaja Adiwoso, A., Erri Astoeti, T., Marks, L. 2013. Oral health condition and treatment needs among young athletes with intellectual disabilities in Indonesia. *International Journal of Paediatric Dentistry*. 23(6):408–414. doi:10.1111/ipd.12010.

455. Tsukamoto, M. & Yokoyama, T. 2015. Alternative methods for nasotracheal intubation and extubation in a patient with Apert syndrome. *Anesthesia Progress.* 62:122–124. doi: 10.2344/0003-3006-62.3.122.

456. Tumminelli, G., Di Donato, I., Guida, V., Rufa, A., De Luca, A.,Federico, A. 2015. Oculodentodigital dysplasia with massive brain calcification and a new mutation of *GJA1* gene. *Journal of Alzheimer's Disease*. 49(1):27–30. doi:10.3233/jad-150424.

457. Tuna, E.B., Marşan, G., Gençay, K., Seymen, F. 2012. Craniofacial and dental characteristics of Kabuki syndrome: nine years cephalometric follow-up. *Journal of Clinical Pediatric Dentistry*. 36(4):393–400.

458. Tylki-Szymańska, A. 2014. Mucopolysaccharidosis type II, Hunter's syndrome. *Pediatric Endocrinology Reviews*. 12:107–113. doi:10.1001/archderm.102.5.578.

459. Ufomata D. 1988. Microdontia of a mandibular second premolar. *Oral Surgery, Oral Medicine, Oral Pathology*. 65(5):637–638.

460. Ulualp, S.O., Wright, C.G., Pawlowski, K.S., Roland, P.S. 2004. Histopathological basis of hearing impairment in Wolf-Hirschhorn syndrome. *The Laryngoscope*. 114(8):1426–1430. doi:10.1097/00005537-200408000-00021.

461. UNAIDS. 2010. *UNAIDS Global report 2010 | UNAIDS Report on the Global AIDS Epidemic 2010*. Available at: http://www.unaids.org/globalreport/Global_report.htm

462. UNAIDS. 2014. *South Africa | UNAIDS/. (2014):2014–2015*. Available at: http://www.unaids.org/en/regionscountries/countries/southafrica

463. UNICEF. 2016. *UNICEF Eastern and Southern Africa - HIV and AIDS – Overview.* Available at: https://www.unicef.org/esaro/5482_HIV_AIDS.html

464. Unkel, J.H., Edwards, J.S., Piscitelli, W.P., Tye, G.W. 2012. Dental surgery and anesthetic precautions of a patient with Down syndrome and juvenile rheumatoid arthritis: a case report. *Pediatric Dentistry*. 34(7):517–520.

465. Urban, M.F., Stewart, C., Ruppelt, T., Geerts, L. 2011. Effectiveness of prenatal screening for Down syndrome on the basis of maternal age in Cape Town. *South African Medical Journal*. 101(1):45–48.

466. Uys, H.H.M. & Basson, A.A. 1991. *Research methodology in nursing*. 2nd ed. Pretoria, South Africa: Haum.

467. Valadares, E.R., Carneiro, T.B., Santos, P.M., Oliveira, A.C., Zabel, B. 2014. What is new in genetics and osteogenesis imperfecta classification? *Jornal de Pediatria*. 90(6):536–541. doi: 10.1016/j.jped.2014.05.003.

468. van der Linden, M.S., Vucic, S., van Marrewijk, D.J.F., Ongkosuwito, E.M. 2017. Dental development in Down syndrome and healthy children: a comparative study using the Demirjian method. *Orthodontics & Craniofacial Research*. 20(2):65–70. doi:10.1111/ocr.12139.

469. van Marrewijk, D.J.F., van Stiphout, M.A.E., Reuland-Bosma, W., Bronkhorst, E.M. & Ongkosuwito, E.M. 2016. The relationship between craniofacial development and hypodontia in patients with Down syndrome. *European Journal of Orthodontics*. 38(2):178–183. doi:10.1093/ejo/cjv054.

470. van Well, G.T.J., Paes, B.F., Terwee, C.B., Springer, P., Roord, J.J., Donald, P.R., van Furth, A.M., Schoeman, J.F. 2009. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the Western Cape of South Africa. *Pediatrics*. 123(1): e1–e8. doi:10.1542/peds.2008-1353.

471. van Wyk, P. & van Wyk, C. 2004. Oral health in South Africa. *International Dental Journal*. 54:373–377.

472. Vaughan, R.W. & Wise, L. 1976. Intraoperative Arterial oxygenation in obese patients. *Annals of Surgery*. 184(1):35–42.

473. Vehkalahti, M., Paunio, I. 1994. Association between root caries occurrence and periodontal state. *Caries Research*. 28 (4):301–306. doi:10.1159/000261990

474. Vellappally, S., Gardens, S.J., Al Kheraif, A.A., Krishna, M., Babu, S., Hashem, M., Jacob, V., Anil, S. 2014. The prevalence of malocclusion and its association with dental caries among 12-18-year-old disabled adolescents. *BMC Oral Health*. 14:123. doi:10.1186/1472-6831-14-123.

475. Verhaegh, B.P.M., de Vries, F., Masclee, A.A.M., Keshavarzian, A., de Boer, A., Souverein, P.C., Pierik, M.J., Jonkers, D.M.A.E. 2016. High risk of drug-induced microscopic colitis with concomitant use of NSAIDS and proton pump inhibitors. *Alimentary Pharmacology & Therapeutics*. 43(9):1004–1013. doi:10.1111/apt.13583.

476. Verrotti, A., Agostinelli, S., Cirillo, C., D'Egidio, C., Mohn, A., Boncimino, A., Coppola, G., Spalice, A., et al. 2011.Long-term outcome of epilepsy in Kabuki syndrome.*Seizure*. 20(8):650–4. doi: 10.1016/j.seizure.2011.06.005.

477. Vesseur, A., Cillessen,E & Mylanus, E. 2016. Cochlear Implantation in a patient with Kabuki syndrome. *Journal of International Advanced Otology*. 12(1):129–131. doi:10.5152/iao.2016.2004.

478. Vieira, G.M., Franco, E.J., da Rocha, D.F.P., de Oliveira, L.A., Amorim, R.F.B. 2015. Alternative treatment for open bite class III malocclusion in a child with Williams-Beuren syndrome.*Journal of Orthodontics*. 20(1):97–107. doi: 10.1590/2176-9451.20.1.097-107.oar.

479. Vigild, M. 1985. Prevalence of malocclusion in mentally retarded young adults. *Community Dentistry and Oral Epidemiology*. 13(3):183–184. doi: 10.1111/j.1600-0528. 1985.tb00441. x.

480. Villaverde, M.M. & Da Silva, J.A. 1971. Sotos syndrome: hypertelorism, antimongoloid slant of eye, and high arched palate complex. *Journal of the Medical Society of New Jersey*. 68(10):805–808.

481. Vincent, C., Mercier, J.M. & David, A. 2008. Cleft palate and Williams syndrome. [Abstract]. *Revue De Stomatologie et de Chirurgie Maxillo-faciale*. 109(1):44–47. doi: 10.1016/j.stomax.2007.10.005.

482. Vorster, A., Beighton, P., Chetty, M., Ganie, Y., Henderson, B., Honey, E., Maré, P., Thompson, D., et al., 2017. Osteogenesis imperfecta type 3 in South Africa: Causative mutations in FKBP10*. South African Medical Journal*.107(5), 457-462. doi:10.7196/SAMJ. 2017.v107i5.9461

483. Wadenya, R.O., Stout, A.M., Gupta, A.,Monge, J. 2010. Hurler syndrome: a case report of a 5-year follow-up of dental findings after bone marrow transplantation. *Special Care in Dentistry*. 30(1):14–17. doi:10.1111/j.1754-4505.2009.00115. x.

484. Walia, H., Ruda, J. & Tobias, J.D. 2016. Sevoflurane and bradycardia in infants with trisomy 21: a case report and review of the literature. *International Journal of Pediatric Otorhinolaryngology*. 80:5–7. doi: 10.1016/j.ijporl.2015.11.007.

485. Walker, R.W.M., Colovic, V., Robinson, D.N., Dearlove, O.R. 2003. Postobstructive pulmonary oedema during anaesthesia in children with mucopolysaccharidoses. *Paediatric Anaesthesia*. 13(5):441–447. doi: 10.1046/j.1460-9592.2003.00969. x.

486. Wallace, J.L., Syer, S., Denou, E., De Palma, G., Vong, L., McKnight, W., Jury, J., Bolla, M., et al. 2011. Proton pump inhibitors exacerbate NSAID-induced small intestinal injury by inducing dysbiosis. *Gastroenterology*. 141(4):1314–1322.e5 doi: 10.1053/j.gastro.2011.06.075

487. Waltz, C.F. & Bausell, R.B. 1981. Nur*sing Research: Design, Statistics, and Computer Analysis.*Philadelphia, United States of America: F.A. Davis Co.

488. Wang, J., Sun, K., Shen, Y., Xu, Y., Xie, J., Huang, R., Zhang, Y., Xu, C., et al. 2016. DNA methylation is critical for tooth agenesis: implications for sporadic non-syndromic anodontia and hypodontia. *Scientific Reports*. 6(301):19162. doi:10.1038/srep19162.

489. Wasersprung, D. & Sarnat, H. 2006. Coffin-Lowry syndrome: findings and dental treatment. *Special Care in Dentistry*. 26(5):220–224. doi:10.1111/j.1754-4505. 2006.tb01442. x.

490. Watt-Smith, P. & Walton, G. 2007. A case study on the use of turntable transfer. *Journal of Disability & Oral Health*. 8(3):132–134.

491. Weidlich, P., Cimões, R., Pannuti, C.M., Oppermann, R.V. 2008. Association between periodontal diseases and systemic diseases. *Brazilian Oral Research*. 22 (S1): 32–43.

492. Wiener, R.C. 2015. Dental Fear and Delayed Dental Care in Appalachia-West Virginia. *American Dental Hygienists Association*. 89(4): 274–281.

493. Welbury, T.A. & Welbury, R.R. 1999. Incontinentia pigmenti (Bloch-Sulzberger syndrome): report of case. *ASDC Journal of Dentistry for Children*. 66(3):213–215, 155.

494. Western Cape Government. 2006. *Valkenberg Hospital: The New Admission Unit*. Available: https://www.westerncape.gov.za/news/valkenberg-hospital-new-admission-unit [2016, January 01].

495. Western Cape Provincial Treasury. 2012. Regional Development Profile: City of Cape Town Working paper.57.Available at: https://www.westerncape.gov.za/assets/departments/treasury/dc0_city_of_cape_town_sep-lg_profile_02_2013.pdf

496. Whitaker, S. 2008. Intellectual disability: a concept in need of revision? *British Journal of Development Disabilities*. 54(106):3–9. doi:10.1179/096979508799103350.

497. White, J.A. & Beltran, E.D. & Perlman, S., 2004. Training Manual for Standardized Oral Health Screening Training Manual for Standardized Oral Health Screening. Availble: http://media.specialolympics.org/resources/health/disciplines/specialsmiles/Special-Smiles-Training-Manual.pdf.

498. Whitman, B.Y., Myers, S., Carrel, A.,Allen, D. 2002. The behavioral impact of growth hormone treatment for children and adolescents with Prader-Willi syndrome: a 2-year, controlled study. *Pediatrics*. 109(2):E35. Available at: http://pediatrics.aappublications.org/content/109/2/e35

499. Williams, A.N. 2002. “Of stupidity or folly”: Thomas Willis’s perspective on mental retardation. *Archives of Disease in Childhood*. 87(6):555–557.

500. Williams, C. 2014. Anesthetic management of Costello syndrome: a case report. *American Association of Nurse Anesthetists*. 82(2):108–113.

501. Winter, K., Baccaglini, L. & Tomar, S. 2008. A review of malocclusion among individuals with mental and physical disabilities. *Special Care in Dentistry*.28(1):19–26. doi:10.1111/j.1754-4505.2008.00005.x.

502. Wisdom, J. & Creswell, J.W. 2013. Mix*ed Methods: Integrating Quantitative and Qualitative Data Collection and analysis while studying patient-centered medical home models. A*vailable: https://pcmh.ahrq.gov/sites/default/files/attachments/MixedMethods_032513comp.pdf

503. Witkop, C.J. 1988. Amelogenesis imperfecta, dentinogenesis imperfecta and dentin dysplasia revisited: problems in classification. *Journal of Oral Pathology*. 17(9–10):547–553.

504. Wold, S.M., Derkay, C.S., Darrow, D.H.,Proud, V. 2010. Role of the pediatric otolaryngologist in diagnosis and management of children with mucopolysaccharidoses. *International Journal of Pediatric Otorhinolaryngology*. 74(1):27–31. doi: 10.1016/j.ijporl.2009.09.042.

505. Wolf, D.S., Golden, W.C., Hoover-Fong, J., Applegate, C., Cohen, B.A., Germain-Lee, E.L., Goldberg, M.F., Crawford, T.O., et al. 2015. High-dose glucocorticoid therapy in the management of seizures in neonatal Incontinentia pigmenti: a case report.*Journal of Child Neurology*. 30(1):100–6.doi:10.1177/0883073813517509.

506. Wong, D., Ramachandra, S. S., & Singh, A. K. 2015. Dental management of patient with Williams Syndrome - A case report. *Contemporary Clinical Dentistry*, *6*(3), 418–420. http://doi.org/10.4103/0976-237X.161908

507. Wright, A.J., Gomes,T., Mamdani,M.M.,, Horn, J.R., Juurlink, D.N. 2011. The risk of hypotension following co-prescription of macrolide antibiotics and calcium-channel blockers. *Canadian Medical Association Journal*. 183(3):303–307.

508. Wyne, A. 2002. Dental management of mentally retarded patients. *Pakistan Oral & Dental Journal.* 22(1). Available at: http://www.podj.com.pk/PODJ/Vol.%2022%20(1)%20(June%202002)/22_1_03-08.pdf

509. Yano, S., Baskin, B., Bagheri, A., Watanabe, Y., Moseley, K., Nishimura, A., Matsumoto, N.,Ray, P.N. 2011. Familial Simpson-Golabi-Behmel syndrome: studies of X-chromosome inactivation and clinical phenotypes in two female individuals with *GPC3* mutations. *Clinical Genetics*. 80(5):466–571. doi:10.1111/j.1399-0004.2010.01554. x.

510. Yoshikawa, F., Tamaki, Y., Okumura, H., Miwa, Z., Ishikawa, M., Shimoyama, K., Nakamura, Z., Kunimori, H., et al. 2013. Risk factors with intravenous sedation for patients with disabilities. *Anesthesia Progress*. 60(4):153–161. doi:10.2344/0003-3006-60.4.153.

511. Yoshioka, S., Takano, T., Matsuwake, K., Sokoda, T., Takeuchi, Y. 2011. A Japanese patient with Kabuki syndrome and unilateral perisylvian cortical dysplasia. *Brain & Development*. 33(2):174–6. doi: 10.1016/j.braindev.2010.04.001.

512. Yoskovitch, A., Tewfik, T.L., Brouillette, R.T., Schloss, M.D.,Der Kaloustian, V.M. 1998. Acute airway obstruction in Hunter syndrome. *International Journal of Pediatric Otorhinolaryngology*. 44(3):273–278.

513. Young, W., Khan, F., Brandt, R., Savage, N., Razek, A.A., Huang, Q. 2001. Syndromes with salivary dysfunction predispose to tooth wear: case reports of congenital dysfunction of major salivary glands, Prader-Willi, Congenital Rubella, and Sjögren's syndromes. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics.*92(1): 38-48.doi:10.1067/moe.2001.113549.

514. Zhou, G., Schwartz, L.T. & Gopen, Q. 2009. Inner ear anomalies and conductive hearing loss in children with Apert syndrome: an overlooked otologic aspect. *Otology & Neurotology.* 30(2):184–189. doi:10.1097/mao. ob013e318191a352.

515. Ziebolz, D., Rost, C., Schmidt, J., Waldmann-Beushausen, R., Schondube, F.A., Mausberg, R.F., Danner, B.C. 2015. Periodontal bacterial DNA and their link to human cardiac tissue: findings of a pilot study. *Thoracic and Cardiovascular Surgeon*. doi:10.1055/s-0035-1564689. Available at: https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0035-1564689

516. Ziyadeh J, Merrer, L., Robert, M., Arnaud, E., Valayannopoulos, V., Di Rocco, F. 2013. Mucopolysaccharidosis type 1 and craniosynostosis. *Acta Neurochirurgica*. 155(10):1973–1976. doi:10.1007/s00701-013-1831-9.
517. Zollino, M., Orteschi, D., Ruiter, M., Pfundt, R., Steindl, K., Cafiero, C., Ricciardi, S., Contaldo, I., et al. 2014. Unusual *4p16.3* deletions suggest an additional chromosome region for the Wolf-Hirschhorn syndrome-associated seizures disorder. *Epilepsia*. 55(6):849–857. doi:10.1111/epi.12617.
518. Zwierzchowski, T.J., Przedborska, A., Wilmańska, I., Raczkowski, J.W. 2015. Rubinstein-Taybi syndrome in a 19-year old boy. *Neuro Endocrinology Letters*. 36(5):417–420.

Addendum 2

RESEARCH RECORD SHEET

PATIENT DETAILS:

Name: _____

DOB: _____ Gender: _____

Language: _____ Code : _____

Date: _____

Site of examination: _____ File No: _____

Patient address: _____

_____

_____

Contact details: _____

Referred by:_____Tel. No. _____

Specific diagnosis:

_____

Clinical history:

- Pregnancy: _____
- Birth: _____
- Operations: _____

Family history:

- Affected relatives: _____
- Parent cosanguinity: _____

X Rays: _____

Report of findings:

_____

_____

_____

CLINICAL FEATURES:

General condition: _____

Height:_____ Weight:_____ Head circumference: _____

Physical Impairment: _____

Hearing Impairment: _____

Visual Impairment:_____

Systemic conditions: _____

Current medication:_____

Other manifestations:

_____

_____

DENTO/ORO/CRANIOFACIAL FEATURES:

Extra-oral /Facial features:

External Abnormalities: _____

_____

Facial Symmetry: _____

Facial profile:

Covex: _____

Flat: _____

Concave: _____

Maxillary/Mandibular/Protrusive: _____

Maxillary/Mandibular/Retrusive: _____

Lip Posture:

Together relaxed: _____

Together strained: _____

Habits:

Tongue thrust: _____

Lip wedge: _____

Digit sucking: _____

Bruxing: _____

Other: _____

Intra-oral hard tissue /dental findings:

Dentition:

Teeth Present/Absent:

Primary				55	54	53	52	51	61	62	63	64	65			
Secondary	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Secondary	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
Primary				85	84	83	82	81	71	72	73	74	75			

Caries:

Primary				55	54	53	52	51	61	62	63	64	65			
Secondary	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Secondary	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
Primary				85	84	83	82	81	71	72	73	74	75			

Variations in tooth colour\structure: _____

Variations in the size\shape of teeth: _____

Variations in tooth number: _____

Midlines: Relative to mid-sagittal plane: _____

Maxillary: mm (R or L) _____

Mandibular: mm (R or L) _____

Overbite: mm _____

Overjet: mm _____

Frena:

Upper: _____

Lower: _____

Gingival disease: _____

Radiographical Findings: _____

_____

_____

Pathology: _____

_____

_____

_____

Comments: _____

Treatment plan: _____

_____

_____

Intra-oral soft tissue findings:

_____

_____

_____

_____

TO DO (CHECK LIST):

Document clinical findings: _____

Consent forms: _____

Extraoral and Intraoral photographs: _____

Tooth for histology: _____

Imaging: Panorex: _____ Ceph: _____

Cone Beam: _____ EM: _____

Addendum 3

RESEARCH PARTICIPANT INFORMATION SHEET: Parent/Guardian

Study Title: Dental Implications of Genetic and Congenital Intellectual Disability in Cape Town

Principal investigator's name: Dr Tina Roberts

Contact details of principal investigator:

Email: drtsroberts@gmail.com: Phone: 0219373158

Supervisor's name: Professor P Beighton

Dear Parent\Guardian

My name is Tina Roberts. I work with the Division of Human Genetics at the University of Cape Town with children affected by genetic and congenital Intellectual Disability (ID) specifically looking at their teeth. I would like to invite your child to take part in our clinical project.

Before you decide whether or not you wish for your child to take part, you should read the information provided below. Take time to ask questions and don't feel under pressure to make a quick decision.

You should clearly understand the risks and benefits of your child participating in this study. This process is known as 'informed consent'.

Your child does not have to take part in this study. If you decide that you do not wish for him/her to take part it, won't affect your child's medical or dental care.

You can change your mind about your child participating in the study at any time. Even if the study has begun, you can still decide to withdraw your child from the study. You don't have to give a reason. If you do withdraw your child from the study, it won't affect the quality of treatment your child will receive now or in the future. If you withdraw your child from the study, please notify us and we will destroy all his\her records

---

Why is the study being done?

This research study is being done to record the dental features in children with ID in South Africa. In doing so, we would like to identify the dental needs of the affected children. We also hope that the results may help us understand the reasons why certain dental changes occur in ID and how they occur. This will assist us in planning and developing specific dental procedures to manage the dental treatment of children with ID. Also, by asking you certain questions, we will be able to gain an understanding of how dental in the mouth may affect your child's day-to-day activities.

Who will be doing the study and how will it be paid for it?

I, Dr Tina Roberts will be leading this project and will be supervised by Prof Peter Beighton. The project will contribute toward acquiring my PhD. I will not be receiving any money personally, but if I require money for things like travelling allowances for volunteers, I will receive it from Prof Peter Beighton's NRF research fund.

Why is your child being asked to take part?

Your child is being asked to take part because he/she is either attending a special facility for children with ID or your child has been referred to me from the Medical Genetics Department at Red Cross Children's hospital with a diagnosis of ID.

How will the study be carried out\what is required of your child?

The study will involve looking at your child's hospital files, talking to you as parents or guardians and examining your child's mouth. We will do this by having your child sit in a dentist chair, or, if at school, just a normal chair. We will then use a small dental mirror to count his\her teeth to see if they are all there and if they need to be cleaned, filled or extracted or if they need braces. We will also check your child's gums to see if they are

healthy. We will then write down all we discover on a special sheet, giving it a special number so that nobody knows who your child is. If your child needs any treatment, we will arrange for him\her to attend either the dental unit at Red Cross Children's hospital or the University of the Western Cape's Dental Faculty at Tygerberg Hospital where they will be treated. We may also need to take photographs of your child and or X-rays of your child's mouth. These will only be done if you (parent\guardian) agree, if it is necessary and if the facilities are available. The photographs and X-rays will be given the same special number that appears on the paper we wrote the information of your child's mouth. Only my colleagues working on the project and I will know who the information belongs to. The photographs are optional, and If you do not want us to take them, your child, will still be able to take part in the study and receive the same treatment as other volunteers in the study. The X-rays will only be done if it is necessary and help with the treatment.

If your child's tooth needs to be extracted, we will only do so with your permission. If any visible changes are present in extracted tooth, we may send it for special investigation where we will look at it under a microscope.

What are the benefits of taking part in this study?

Although this study will not make your child better, it will help dentists understand the changes in your child's mouth, how they happened and why they happened. It will also help dentist plan your child's future dental treatment. By asking you a few questions about your child's toothbrushing habits, we will discover how the dental problems can affect his\her day to day activity and resolve them at no cost.

By taking part in the study your family will also help other children and families with similar conditions.

What are the risks involved in this study?

There are no, if any risk at all to your child. This study does not involve any injecting or cutting and is painless. No medication will be given to your child.

Will it cost me anything to take part?

There are no costs at all to the research participant. All expenses eg, travel will be paid from research funds.

Is the study confidential?

Written informed consent will be obtained from all participants on standardized

forms which will be available in English, Afrikaans, Xhosa and if necessary any other indigenous language. In the case of minors, consent will be obtained from their parents and where possible, assent will be obtained from children.

- All information will be stored in password protected computers. Written information will be stored in a locked office.
- Anything that may identify you, will be changed when the data are published.
- Photographs will only be used with the eyes hidden and with informed consent.

If you have any further questions or need any further information now or at any time, please contact:

Dr Tina Roberts

Division of Human Genetics

Faculty of Health Sciences, UCT

Office: 021-9373158

Email Address: drtsroberts@gmail.com

For any queries regarding your rights as a volunteer in this study please contact"

Professor Marc Blockman,

Chair,

UCT Human Research Ethics Committee,

Faculty of Health Sciences, UCT

Office: 021-4066492 **Email address: marc.blockman@uct.ac.za**

RESEARCH PARTICIPANT INFORMATION SHEET: Child

Study Title: Dental Implications of Genetic and Congenital Intellectual Disability Cape Town.

Principal investigator's name: Dr Tina Roberts

Contact details of principal investigator: email: drtsroberts@gmail.com: phone: 0219373158

Supervisor's name: Professor P Beighton

Hi There

My name is Tina Roberts. I work with the Division of Human Genetics at the University of Cape Town with children affected by genetic and congenital Intellectual Disability (ID) specifically looking at their teeth. I would like to invite you to take part in a clinical project.

Before you decide whether or not you wish would like to take part, you should read the information provided below. Take time to ask questions and don't feel under pressure to make a quick decision.

You should clearly understand the risks and benefits if you decide to take part in this study. This process is known as 'informed consent'.

Your do not have to take part in this study. If you decide that you do not want to take part, it will not affect your medical or dental care.

You can change your mind about participating in the study at any time. Even if the study has begun, you can still decide to withdraw from the study. You don't have to give a reason. If you do withdraw from the study, it won't affect the quality of treatment you will receive in the future. If you withdraw from the study, please notify us and we will destroy all your records.

Why is the study being done?

This research study is being done to record the dental features in children with genetic and congenital ID. The results of our findings will identify the dental needs of affected children. The results will also help us understand the reasons why certain dental changes may occur in ID and possibly how they occur. This will help us plan and develop specific dental procedures to manage the dental treatment of children with ID. By asking you or your parents\guardian certain questions, we will also be able to gain understanding of how certain changes in the mouth may affect your day-to-day activities.

Who will be doing the study and how will it be paid for it?

I, Dr Tina Roberts will be leading this project and will be supervised by Prof Peter Beighton. The project will is part of my PhD degree. Personally, I will not be receiving any money, but if I need monies, I will receive from Prof Peter Beighton's NRF research fund.

Why are you being asked to take part?

You are being asked to take part because you are either attending a school for children with ID or you have been referred to me from the Medical Genetics Department at Red Cross Children's hospital with a diagnosis of ID.

How will the study be carried out\ What do you need to do?

The study will involve looking at your hospital files, talking to your parents or guardians and examining your mouth. We will do this by having you sit in a dentist chair, or if at school, just a normal chair. We will then use a small dental mirror to count your teeth to see if they are all there and if they need to be cleaned, filled or extracted or if you need braces. We will also check your gums to see if they are healthy. We will then write down all we find on a special

sheet and give it a special number so that nobody knows who you are. If you need any treatment, we will arrange it for you either at the dental unit at Red Cross Children's hospital or at the University of the Western Cape, Dental Faculty. We may also need to take photographs of you and or X-rays of your mouth. These will only be done if you and parent\guardian agree, if it is necessary and if the services are available. The photographs of you and or and X-rays will be given the same special number that appears on the paper we wrote the information of your mouth. Only my colleagues working on the project and I will know who the information belongs to. If you do not want us to take X-rays or photographs, you will still be able to take part in the study and still receive the same treatment as other volunteers in the study.

What are the benefits of the study?

Although this study will not make you better, it will help dentists understand the changes in your mouth, how they happened and why they happened. It will also help dentist plan your future dental treatment. By asking you a few questions about your toothbrushing habits, we will discover how the dental problems can affect your day to day activity and resolve them at no cost.

By taking part in the study your family will also help other children and families with similar conditions.

What are the risks involved in this study?

There are no, if any risk at all to you. This study does not involve any injecting or cutting and is painless. No medication will be given to you.

Will it cost me anything to take part?

There are no costs at all to the research participant. All expenses eg, travel will be paid from research funds.

Is the study confidential?

- Written informed consent will be obtained from all participants on standardized forms which will be available in English, Afrikaans, Xhosa and if necessary any other indigenous language. In the case of minors, consent will be obtained from their parents and where possible, assent will be obtained from children.
- All information will be stored in password protected computers. Written information will be stored in a locked office.
- Anything that may identify you or your family will be changed when the data are published.
- Photographs will only be used with the eyes hidden and with informed consent**.**

If you have any further questions or need any further information now or at any time, please contact:

Dr Tina Roberts

Division of Human Genetics,

Faculty of Health Sciences, UCT

Office: 021-9373158

Email Address: drtsroberts@gmail.com

For any queries regarding your rights as a volunteer in this study please contact"

Professor Marc Blockman,

Chair,

UCT Human Research Ethics Committee,

Faculty of Health Sciences, UCT

Office: 021-4066492 Email address: marc.blockman@uct.ac.za

Addendum 4

Consent

CONSENT FOR PARTICIPATION IN STUDY: (Parent/Guardian-Child)

STUDY TITLE: Dental Implications genetic and congenital Intellectual Disability in Cape Town

1. I (parent/guardian) have read and understood the information sheet about this research project. The information has been fully explained to me and I have been able to ask questions, all of which have been answered to my satisfaction. Yes……. No…….

2. I understand that my child does not have to take part in this study and that I can have him/her withdrawn from the study at any time. I understand that I don't have to give a reason for withdrawing my child from the study and I understand that withdrawing my child won't affect his/her future medical and dental care. Yes……. No…….

3. I am aware of the potential risks of this research study to my child. Yes……. No…….

4. I give permission for researchers to look at my child's medical records to get information. I have been assured that the information about my child will be kept confidential.

Yes……. No…….

5. I (parent/guardian) have been given a copy of the information sheet and this completed consent form. Yes……. No…….

Patient Name (minor): ……

Parent Name: …….

Parent signature: ……..

Child assent (7-17 years): ……

Guardian name: ……

Guardian signature: ……

To be completed by the principal Investigator

I, the undersigned, have taken the time to fully explain to the above patient the nature and purpose of this study in a way that they could understand. I have explained the risks involved as well as the possible benefits. I have invited them to ask questions on any aspect of the study that concerned them.

Principal Investigator Name: ……

Qualifications: ……

Signature: ……

Date: ……

NB: three copies to be made:

- Research participant
- Principal Investigator
- Institution records

PATIENT CONSENT TO CLINICAL PHOTOGRAPHS AND PUBLICATION: (Parent/Guardian – Child)

TO WHOM IT MAY CONCERN

I, the undersigned

……in my capacity as parent/guardian consent to photographs being taken of ……as requested. I understand that these photographs will be stored appropriately, treated with the utmost confidentiality and be part of my child's dental records.

I hereby give consent for the images of my child to be used ONLY for that I have indicated with a tick:

_____Record purposes and for my child's future management

The photographic images will form part of the information collected for your child's care and treatment and will be kept confidential at all times.

_____Education and Training purposes

The photographic images maybe used for teaching purposes and viewed by health professionals outside of the UWC Faculty of Dentistry. The images may be used in talks, conference presentations, posters or on the Internet to help train other health professionals in the management of dental and oral diseases

___Approved research purposes and publications

This may involve the photographic images being used in medical or dental publications, journals, textbooks, conference material, e-publications and on the Internet. Images will be seen by health professionals and researchers who use the publications in their professional education. The images may be seen by the general public. Images will not be used with identifying information such as name, however, full confidentiality is not guaranteed.

___Other Purposes (please specify): ……..

- I understand that all efforts will be made to conceal my child's identity but that full confidentiality cannot be guaranteed
- I understand that my consent or refusal will in no way affect my child's dental care

Patient Name (print)……

Parent/Guardian if patient is under 18 years of age (print name): ……

Parent/Guardian Signature: ……

Date: ……

Child assent (7-17 years): ……..

Principal Investigator print name: ……..

Principal Investigator signature: ……..

Date: ……..

Requesting Clinician name (print)……

Date: …… Department: …….. Phone: ……

Patient Name (print): ……

Views Required: ……

Required for (tick): Records_____ Teaching/ Lectures_____ Research_____ Publication _____

Images taken by: …….. Date: ……..

Location where copies are stored: ……

Addendum 5

Ethics Approval

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Faculty of Health Sciences Human Research Ethics Committee
Room E12-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
e-mail: sumayah.arlefdien@uct.ac.za
www.health.uct.ac.za/research/humanethics/forms

10 May 2013

HREC REF: 204/2013

Dr T Roberts
c/o Prof P Beighton
Human Genetics
FHS

Dear Dr Roberts

PROJECT TITLE: DENTAL IMPLICATIONS OF GENETIC AND CONGENITAL INTELLECTUAL DISABILITY IN CAPE TOWN

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has formally approved the above mentioned study.

Approval is granted for one year till the 15 May 2014.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

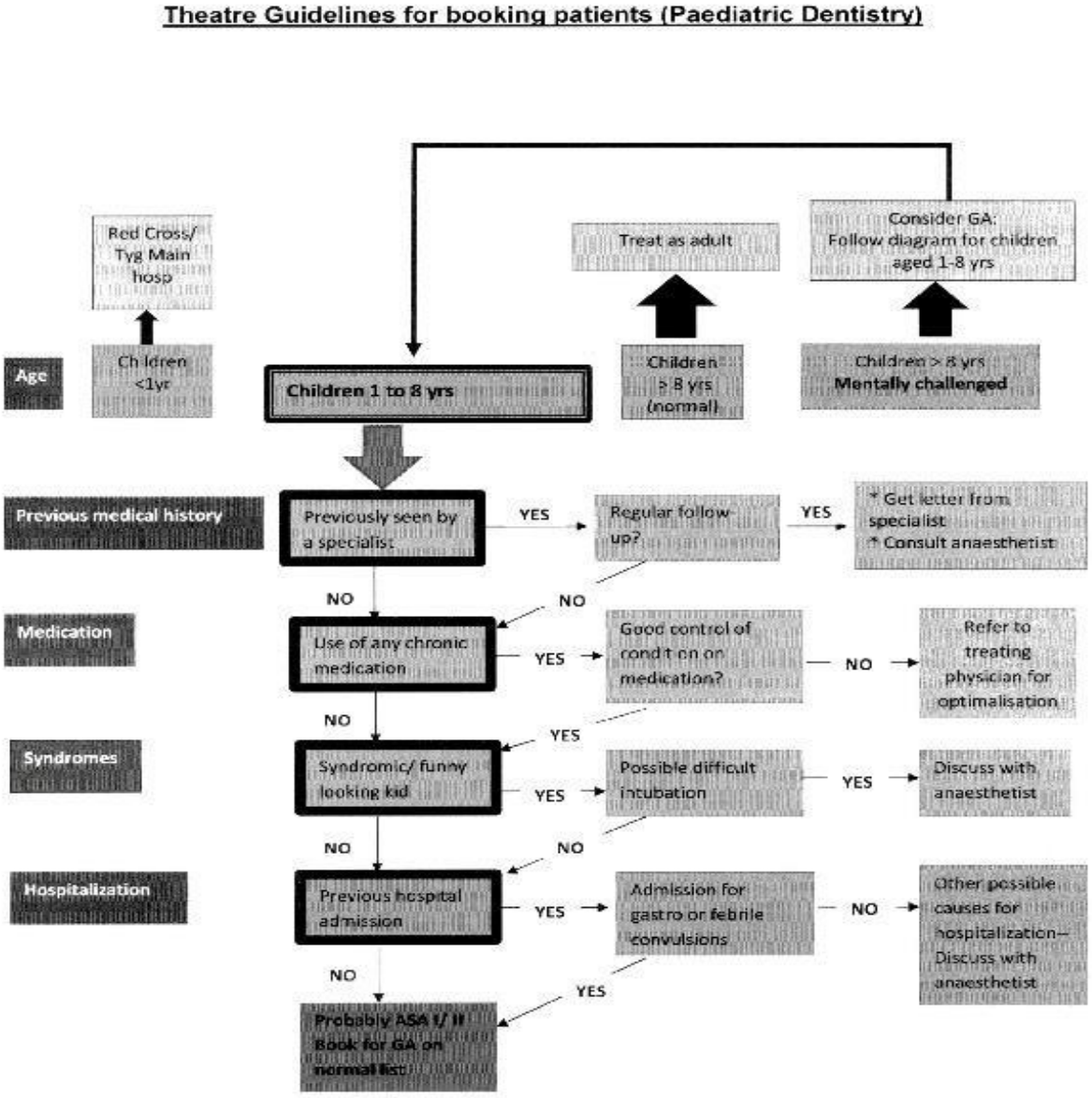
PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA),

Addendum 6

Dental GA protocol



Addendum 7

Protocol for Conscious Sedation (UWC dental)

Patient Selection

Patients are selected according to the following criteria:-

- Traditional techniques unsuccessful in managing behaviour
- Patient is ASA 1 or 2(Guidelines for classifying the baseline health status according to the ASA)
- Patient below age of reason (pre- or uncooperative)
- Extent of treatment
- Needle phobic; excessively fearful older child
- Older child with poor experiences or coping abilities
- Developmental delay or handicapping condition/ medical problem

History

The following conditions might influence the sedation outcomes and must be assessed:-

- Allergies/asthma/croup must be considered
- Current meds including over the counter may include depressants
- Diseases - CV, CNS, pulmonary, liver, kidney, pregnancy status
- Family history of diseases
- Sleep apnea - snoring suggests tonsil/airway problem
- Previous sedations/GA/hospitalization

Physical Assessment

A thorough physical assessment is required by taking the following into consideration:-

- General physical condition (gait, wheelchair, coordination)
- Vital signs—HR, RR, BP
- Vital statistics - age and weight
- Airway—tonsils, neck, nose, tongue must not be potential airway obstacle
- Mouth breather/C-spine/nasal speech
- Midfacial hypoplasia
- Risk assessment - ASA status III, IV contraindicated
- Obesity
- Communication ability

The safe sedation of children for procedures requires a systematic approach that includes the following:

- No administration of sedating medication without the safety net of medical supervision;
- Careful pre-sedation evaluation for underlying medical or surgical conditions that would place the child at increased risk from sedating medications;
- Appropriate fasting for elective procedures and a balance between depth of sedation and risk for those who are unable to fast because of the urgent nature of the procedure
- A focused airway examination for large tonsils or
- Anatomic airway abnormalities that might increase the potential for airway obstruction;
- A clear understanding of the pharmacokinetic and pharma-dynamic effects of the medications used for sedation, as well as an appreciation for drug interactions
- Appropriate training and skills in airway management to allow rescue of the patient; age- and size-appropriate equipment for airway management and venous access
- Appropriate medications and reversal agents;
- Sufficient numbers of people to carry out the procedure and monitor the patient;
- Appropriate physiologic monitoring during and after the procedure;
- A properly equipped and staffed recovery area;
- Recovery to pre-sedation level of consciousness before discharge from medical supervision; and appropriate discharge instructions.

Documentation required before sedation

1. **Informed consent**: the patient record shall document that appropriate informed consent was obtained according to the institutional requirements.
2. **Instructions and information provided to the responsible person**: the practitioner shall provide verbal and/or written instructions to the responsible person.

CLINICAL PROTOCOL FOR SEDATION AT TYGERBERG ORAL HEALTH CENTRE