TUBERCULOSIS IN THE HEAD AND NECK – EXPERIENCE IN DURBAN, KWAZULU-NATAL

by

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A thesis submitted in partial fulfilment of the requirements for the degree of MSc (Dent) in Dental Public Health, University of the Western Cape

September 2009

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ABSTRACT

Tuberculosis is the world's leading cause of death from a single infective agent. The World Health Organisation has declared the disease a "global emergency". Extra-pulmonary presentations form a major proportion of new cases, especially since the advent of the acquired immunodeficiency syndrome epidemic. Therefore, it is important that oral health care workers are aware of tuberculosis in the head and neck region and its varied manifestations. This study reports on one hundred and four patients diagnosed with tuberculosis and with head and neck tuberculosis lesions.

The aim of the study was to determine the extent to which tuberculosis presents in the head and neck region. It was a descriptive, retrospective, record-based study on a cohort of tuberculosis patients that presented with head and neck tuberculosis at private practices in the Durban area over a fourteen month period. A structured data capture sheet was the method chosen for recording the data.

The majority of the sample (89.4%) had tuberculosis of the head and neck lymph nodes, five (4.8%) had tuberculosis of the tonsil, two (1.9%) had tuberculosis of the larynx, two (1.9%) had tuberculosis of the ear, one (1%) had parotid gland tuberculosis and one (1%) had tuberculosis of the nose. The records indicate that excision biopsy and histopathological examinations were used to make a diagnosis. A third (33.7%) of the patients were confirmed with human immunodeficiency virus infection.

A high index of suspicion of tuberculosis is important in the differential diagnosis of neck swellings, hoarseness and otorrhoea and in human immunodeficiency virus positive patients with an enlarging neck mass. A biopsy is usually necessary for diagnosis. Successful outcome depends upon appropriate chemotherapy and timely surgical intervention when necessary. Oral health care workers need to be fully cognizant of all the various presentations of head and neck tuberculosis to allow early diagnosis and quick commencement of appropriate treatment.

Keywords: Head and neck, Tuberculosis, HIV, Oral health care workers, cervical lymph nodes, extra-pulmonary.

DECLARATION

I, Moganavelli Reddy, the undersigned, hereby declare that the thesis entitled "Tuberculosis in the head and neck region – experience in Durban, Kwa-Zulu Natal" is my original work, that it has not been previously in its entirety or in part submitted for any degree or examination at any other University, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

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Moganavelli Reddy Date

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to the following individuals, institutions and facilities for their assistance in the preparation of this dissertation:

My sponsor, Professor Aubrey Sheiham, for the scholarship which made my postgraduate studies a reality.

My profound gratitude goes to Professor Sudeshni Naidoo for her relentless support, encouragement and assistance throughout the course of the program. Despite her very busy schedule she took the time to read, critique and advise in all aspects of the preparation of this dissertation.

My sincere thanks to Mr Logan Govender and staff of the Lancet laboratory, without whose permission and assistance this project would not have been possible.

My sincere gratitude to Drs Ramjettan, Peer, Thander, Mansab, Sarvan Mohamed, Charles, Rajput, Latiff, Raidoo, IS Vawda, Bhoola, AG Naidu, Jeena, D Maharaj, A Osman, Cassim, ADR Reddy, B Govender and D Govender for willingly allowing me access to their patient records and to their staff for all their assistance.

I would also like to express my sincere gratitude and appreciation to the Head of the School of Dentistry – University of Kwa-Zulu-Natal, Dr PK Singh for her encouragement and support throughout my studies. Thanks also to my colleague, Dr S Singh, for her encouragement and assistance throughout my studies.

My eternal gratitude and thanks goes to my husband Kevin and my family for their love, support, encouragement and understanding.

God bless you all

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LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ARVs	Anti-retrovirals
ART	Anti-retroviral treatment
BCG	Bacille Calmette-Guérin
CDC	Centres for Disease Control and Prevention
DOH	Department of Health
DOTS	Directly observed treatment short course
ENT	Ear nose and throat
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
M	Mycobacterium
MD-R	Multi-drug resistant
PPD	Purified protein derivative
TMJ	Tempero-mandibular joint
TB	Tuberculosis
USAID	United States Agency for International Development
XDR	Extensively drug resistant

CHAPTER 1: INTRODUCTION

Tuberculosis (TB) is a highly infectious, debilitating disease that typically involves the pulmonary system, but can affect any organ or tissue, including the mouth (Randy *et al*. 1993). While TB notification rates continue to decrease in many parts of the world, rates have increased more than three-fold in many countries in sub-Saharan Africa since 1990, fuelling a 1% increase in global TB incidence (WHO, 2008). In 1993, it was the world's leading cause of death from a single infectious agent. The World Health Organisation (WHO) declared the disease "a global health emergency" (Williams and Jones 1995: 5). In 2005 the African continent, with just 11% of the world's population, accounted for 27% of the global burden of TB and 30% of TB related deaths. Over two million new TB cases and over 500 000 TB-related deaths are estimated to occur in the region annually (Corbett *et al*. 2003). Factors that influenced the resurgence of the disease included the emergence of multidrug-resistant (MDR) organisms, social deprivation (injection drug use, homelessness, poverty), reduced priority to TB control, the increasing population of young adults that constituted the majority of the infected subjects, immigration from endemic areas, deteriorating health care infrastructures and the Acquired Immune Deficiency Syndrome (AIDS) pandemic.

Every year about 8–10 million people are infected with *Mycobacterium tuberculosis* (*M. tuberculosis)* and 2 million die from it. About a third of the world's population (about 2 billion people) carries the TB bacteria, but most never develop the active disease (WHO, 2000). Around 10% of people infected with TB actually develop the disease in their lifetime, but this number is increasing due to the human immunodeficiency virus (HIV) that severely weakens the human immune system and makes people more vulnerable to infections. Disease caused by the relatively non-virulent non-tuberculosis mycobacteria, such as *Mycobacterium avium* complex, tends to affect only those with very low CD4 lymphocyte counts. In contrast, the risk of TB increases after HIV seroconversion and is elevated across the full spectrum of immunodeficiency, increasing steeply as the CD4 count declines.

The impact of HIV on the TB epidemic is potentially catastrophic: HIV increases the susceptibility of the HIV positive person to TB. The advent of HIV has resulted in 5 – 10% *annual* risk of developing TB as compared with 5 – 10% *lifetime* risk of TB infection in people without HIV (WHO, 2000). About 50% of TB patients in South Africa are infected with HIV (Department of Health (DOH), 2006). HIV-infected persons not only have high rates of reactivation TB, but also have heightened susceptibility to new exogenous infection and rapidly progressive primary disease. Genetic fingerprinting studies have shown that high TB recurrence rates are fuelled by a high rate of exogenous reinfection. Nosocomial transmission of TB among HIV-infected individuals is a major hazard as was illustrated by the recent outbreak of extensive drug resistant (XDR) TB in Kwa-Zulu-Natal in 2006 (Andrews *et al*. 2008).

Tuberculosis infections are acquired by inhalation of the tubercle bacilli that are present in airborne particles. TB of the respiratory tract is the most infective form. Prior to the HIV epidemic, 85% of reported TB cases were limited to the lungs. This has now changed particularly in HIV infected individuals as extra-pulmonary TB tends to increase in frequency if immune function is compromised.

With the decrease in the general incidence of head and neck involvement to a point where it was often taken as a rare finding, clinicians were not “sensitized” to the head and neck manifestations as part of a differential diagnosis. This has often resulted in a delay in the diagnosis and therapy or the diagnosis being missed entirely. After a decline for several decades, the incidence of mycobacterial disease as a whole, and the extra-pulmonary type in particular, is on the rise in many regions of the world. TB often presents in the head and neck with the cervical lymph nodes being one of the commonest sites of extra-pulmonary TB (Williams and Jones, 1995). Head and neck TB also presents in the oral cavity, nose, ears, larynx, thyroid and salivary glands, but these locations are rare.

More recently, strains of TB resistant to all major anti-TB drugs have emerged. Drug-resistant TB is caused by inconsistent or partial treatment, when patients do not take their medicines regularly for the required period because they start to feel better, because doctors and health workers prescribe the wrong treatment regimens or because the drug supply is unreliable. A particularly dangerous form of drug-resistant

TB is MDR TB which is resistant to the two most powerful anti-TB drugs, isoniazid and rifampicin (Weyer, 2005).

The emergence of XDR TB, especially where many TB patients are also infected with HIV is a serious threat to TB control. The Stop TB Strategy was launched by the WHO in 2006. The six major components that were included were the (i) Directly Observed Treatment, Short-Course (DOTS) expansion and enhancement, (ii) addressing TB/HIV, MDR-TB and other challenges, (iii) contributing to health system strengthening, (iv) engaging all care providers, (v) empowering patients, and communities, and (vi) enabling and promoting research (WHO, 2008).

M. tuberculosis is uniquely hazardous to oral health care workers because of its airborne route of transmission. The resurgence of TB as a public heath problem has rekindled interest in the disease among oral health care workers. However, much research has focused on pulmonary and extra-pulmonary TB (excluding head and neck) and there is a paucity of literature on the head and neck region. In some instances, systemic symptoms of TB may be absent, and head and neck lesions may be the first manifestation of the disease, therefore oral health care workers need to be aware of TB in the head and neck region and its varied manifestations.

CHAPTER 2: LITERATURE REVIEW

This chapter reviews the literature related to the history of TB in South Africa, its co-existence with HIV, the epidemiology, aetiology, pathology and pathogenesis of TB and the clinical features of pulmonary disease. It also discusses the presentations in the head and neck region. In addition, the diagnosis, risk factors, treatment control and prevention are described. The importance of TB to oral health care workers is also highlighted.

2.1 BACKGROUND

In the early 1960s, Sir MacFarlane Burnet said, “One can think of the middle of the twentieth century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious diseases as a significant factor in social life” (Burnet, 1962). This was not an uncommon sentiment among the medical community and resulted in a decrease in awareness, research, and funding to combat emerging, re-emerging and drug resistant infections. Consequently, the medical community was ill-prepared when diseases thought to have disappeared, and new diseases, started to emerge in the 1980s and 1990s.

In a recent report from the Institute of Medicine (Institute of Medicine, 1992), six major factors were identified as contributors to the emergence and re-emergence of infectious diseases: (i) changes in human demographics and behaviour, (ii) advances in technology and changes in industry practices, (iii) economic development and changes in land use patterns, (iv) dramatic increases in volume and speed of international travel and commerce, (v) microbial adaptation and change and (vi) breakdown in public health capacity required to handle infectious diseases.

Although the number of deaths from infectious diseases had decreased dramatically during the twentieth century, there has been an increase from 1980, mainly due to the emergence of the HIV (Centres for Disease Control and Prevention (CDC), 1999). HIV and other emerging and re-emerging infectious diseases are recognised as

significant health hazards and have become the focus of many international and national health initiatives.

Efforts at controlling infectious diseases have addressed sanitation and hygiene, vaccination, the use of antibiotics and other antimicrobial medications and improved technology in detection and monitoring. Oral health care workers are not excluded from these efforts, as many of these endeavours impact directly on dental care.

2.2 TUBERCULOSIS GLOBALLY INCLUDING SOUTH AFRICA

2.2.1 History

TB is a widespread scourge that can be traced back to the earliest of centuries. During the 17th century, colonialists, settlers and missionaries from Europe and North America who were infected with TB arrived in South Africa. They were seeking a cure from the sun and fresh air. The previously unexposed and non-immune South African population rapidly developed TB (Edginton, 2000).

Workers in the gold mines on the Reef in the 1800s were exposed to silica dust, overcrowded hostel living, poor nutritional status and stress, all of which were major contributors to the development of TB. They returned to their families in the rural areas when they became sick and spread the disease to the community. It was estimated that over 60% of the black population of South Africa was infected by 1930. The rate of active disease in 1953 was measured to be 780 per 100 000 of the population of the northern and eastern parts of the country (Edginton, 2000). Apartheid policies were responsible for much of the TB manifestations during this era. Rural poverty and rapid urbanisation created living conditions that were conducive to the continuing epidemic. This was uncontrolled because health services were inadequate for the majority of the population. Poorly funded and inadequate health services were directly responsible for under-treatment of patients during apartheid (Edginton, 2000).

2.2.2 Present Situation

TB remains the most important communicable disease in the world and in South Africa it accounts for 80% of all notifiable diseases (Edginton, 2000). The annual number of new cases averages 380/100 000 population – even in other hard hit parts of the world, the average is only about 200 per 100 000.

The TB epidemic in South Africa is one of the worst in the world, with certain impoverished areas having the fastest growing epidemic than anywhere else in the world. Nearly two thirds of the population in the country are infected with TB, 160 000 South Africans from all walks of life become ill with TB every year and about 10 000 people die of TB every year. Poorer communities appear to be at greater risk of exposure and to chronic TB infection (DOH, 1996). TB has been common in South Africa since colonisation and early urbanization. The notification rate has varied from around 50/100 000 in the 1920s, increasing to about 350/100 000 in 1965 followed by a decrease until 1988 when the notification rate was 172/100 000. In 2004 the national incidence rate was an alarming 718/100 000 – a major increase from 338 per 100 000 in 1998 (Erstad, 2006).

TB is a major public health problem in South Africa. In 2006, the WHO ranked South Africa fifth among the world's 22 high-burden TB countries (United States Agency for International Development (USAID), 2006). The TB epidemic in South Africa is likely to be exacerbated over the next few years due to the high prevalence of HIV/AIDS. TB-HIV co-infection rates are high, with as many as 60 percent of adult TB patients being HIV-positive (USAID, 2006). MDR TB, largely caused by non-adherence to drug regimens or inappropriate drug regimens, is further exacerbating the epidemic. National studies of MDR-TB conducted by the Medical Research Council of South Africa in 2002 found that 1.6 percent of new TB cases and 6.7 percent of re-treatment cases had MDR-TB (USAID, 2006).

The proportion of people with extra-pulmonary TB has also trebled, but appears to have stabilised at around 15% (DOH, 2006). Despite a global slowing down in new TB cases since 2003, South Africa recorded the world's second highest rate of new cases (incidence rate) in 2006 after Swaziland. The World Health Organisation report

in 2006 revealed that 218 people per 100 000 died of TB in South Africa. This was more than in any other country in the world (Cullinan, 2008). The problem of TB in South Africa is largely a result of historical neglect and poor management systems, compounded by the legacy of fragmented health services (Fourie, 2006).

In South Africa, attention has been refocused on the factors associated with the observed reversal of previous declining disease trends, transmission modes of *M. tuberculosis,* occupational risk factors and airborne infection control precautions (Porteous and Terezhalmy, 2008; CDC, 1998; American Thoracic Society, 1992; Bernardo, 1991; CDC, 1991; CDC, 1986). Despite dramatic improvements in public health measures associated with *M. tuberculosis* infection and disease, such as living conditions, nutrition and antimicrobial chemotherapy, TB remains a major public health problem for much of the world's population (WHO, 1997; Dolin *et al*. 1994).

2.2.3 HIV and TB Co-infection

The impact of HIV on the TB epidemic has been catastrophic. HIV increases the susceptibility of the HIV positive person to TB. TB is 500 times more common in HIV-infected than in the normal population. 80% of affected patients develop extra-pulmonary disease (Prasad *et al*. 2007; WHO, 2007; Singh *et al*. 1998; De Cock *et al*. 1992).

Of the 36 million HIV infected persons in the world, one third are co-infected with *M. tuberculosis* and 75% of these people reside in sub-Saharan Africa (Davidsons, 2002). Latent infections present in HIV patients have a 7-10% annual risk of reactivation compared to a 5-10% lifetime risk in an HIV uninfected patient. They have a 10-20% chance of acquiring TB from an open contact compared to 5-10% in a non-HIV patient and a 30-40% chance of developing progressive primary disease as compared to 5-10% in a non-HIV individual. More than 60% of HIV infected patients can develop disseminated miliary or extra-pulmonary disease compared to less than 25% in non-HIV patients. The escalation in TB case rates in sub-Saharan Africa is largely attributable to the explosive HIV epidemic. The annual new case (8 million) and death (2 million) rates in sub-Saharan Africa are expected to continue to rise (Davidsons, 2002).

HIV critically impairs cell-mediated host responses to *M. tuberculosis.* In the immune system, CD4 lymphocytes defend the body against TB. Examination of bronchoalveolar lavage fluid from tuberculous lung segments in HIV infected patients reveals failure of recruitment and activation of CD4 lymphocytes (Lawn *et al*. 2002). Numeric depletion and functional impairment of these cells and disruption of CD4 lymphocyte macrophage interactions result in impaired granuloma formation and reduces the immune systems ability to prevent the growth and spread of *M. tuberculosis.* A weakened immune system allows for dissemination of the bacteria to areas other than the lungs, which explains the increased likelihood of extra-pulmonary TB among HIV positive individuals (Achmat and Roberts, 2005). At the recent conference of the Parasitological Society of Southern Africa it was found that the probable link between AIDS and TB could be the results of chronic infection by the helminths worm that downregulates the cellular immune response that is needed to prevent infection by the HIV and *M. tuberculosis.* It was demonstrated that prevention of helminthiasis could be part of the solution to the pandemics of HIV/AIDS and TB (Fincham, 2008).

Radiographic appearances of pulmonary TB in patients with HIV co-infection reflect impairment of the host inflammatory response, with reduced likelihood of cavitation, fibrosis and classical apical disease. Normal chest radiographs are found in approximately 5% of patients with smear positive pulmonary TB. Mediastinal lympadenopathy and non-specific patterns of consolidation are more common (Harries, 1990).

Diagnosis is made by mycobacterial culture of blood, bone marrow or tissue in patients with late stage HIV and low CD4 counts. Quadruple anti-TB combination therapy has a good response. Patients presenting with both HIV infection and TB may have typical clinical and radiographic features of TB. Experienced clinicians in central Africa have noticed a change in the pattern of the disease. Patients produce no sputum or have negative sputum smears, little change in chest radiography, or there may be diffuse pulmonary infiltrates without cavitation. Extra-pulmonary disease appears to be more common – especially in forms where they were previously uncommon (Harries, 1990).

The change in disease pattern has made diagnosis of TB more difficult (Singh *et al*. 1998; Harries, 1990). Extra-pulmonary TB can be difficult to diagnose and differentiation from neoplastic or other inflammatory conditions can be difficult, particularly in mucosal TB involving the larynx, hypopharynx and nasopharynx (Choudhury *et al*. 2005). In view of the high frequency of non-cavitatory pulmonary disease and extrapulmonary forms of TB, sputum smear microscopy has a low sensitivity for diagnosis. Sensitivity is substantially increased by sputum culture, but this is slow and expensive and the necessary infrastructure is not available over much of Africa (Lawn *et al*. 2002).

HIV in the mid-1980s was not a problem in South Africa and the impending threat to the population was largely ignored (Edginton, 2000; WHO, 2000). Reported cases of TB have quadrupled in South Africa since 1988. The prevalence of HIV in South Africa has increased. The proportion of TB in women has increased from 34.9% in 1995 to 43.5% in 2004. As a result of HIV the proportion of TB patients with extra-pulmonary TB is high at 16.1%. The prevalence of HIV in TB patients was 55.3% (WHO, 2005).

As a result of the HIV epidemic in South Africa, Anti-retroviral treatment (ART) has been made available in the public sector. Irrespective of whether they are receiving anti-retrovirals (ARVs), people with HIV are more vulnerable to developing TB (DOH, 2000). The progression of HIV is also hastened by TB. There is no standardised recording and reporting system in place in South Africa for HIV, which has resulted in slow progress in the HIV/TB collaboration, therefore assessing the TB/HIV collaboration is problematic.

TB, which can occur at any time during the course of HIV, most often occurs early in the disease and probably accelerates the progression of HIV disease. The WHO DOTS strategy remains the central component of global TB control strategies. However, while successful in low HIV prevalence settings, this strategy alone has proven insufficient to contain the African TB epidemic in high HIV prevalence countries.

Additional strategies are needed, including intensified or active case-finding in patient populations at high risk of TB, TB preventive therapy (isoniazid prophylaxis for six

months) can be used in HIV positive patients who have positive tuberculin skin tests and who are not already sick with TB (DOH, 2000) and TB patients should receive HIV information and education and should be offered HIV counselling and testing. Ultimately, control of the HIV epidemic is needed to stem the TB epidemic in countries in southern Africa.

2.2.4 Epidemiology

TB remains the most common cause of death from a single microbial agent and is the most common infectious disease in the world. In 1993, TB was resurrected as a major public health problem world-wide after two decades of neglect and the WHO declared TB to be "a global health emergency" (Williams and Jones 1995: 5). In 2006, 9.2 million new cases (139 per 100 000 population) and 1.7 million deaths from TB occurred globally, of which 0.7 million cases and 0.2 million deaths were HIV positive people. TB is a major cause of illness and death especially in Asia and Africa. South Africa ranks fourth in terms of absolute number of cases. The African region has the highest incidence rate per capita (363 per 100 000 population) (WHO, 2008).

The falling global incidence reversed in the mid 1980s in developed and developing nations. The reason for the increasing incidence of pulmonary TB in developed countries was due to HIV (mainly urban), immigration from high prevalence areas, increasing life expectancy of the elderly, social deprivation (injection drug use, homelessness, poverty), drug resistance (MDR-TB) and reduced priority for TB control. In developing countries the increase in incidence was due to HIV (mainly urban), population increase, lack of access to health care, poverty, civil unrest ineffective control programmes and drug resistance (MDR-TB) (Davidsons, 2002). The most serious aspect of the TB epidemic is the emergence of MDR-TB. It is TB that is resistant to at least isoniazid and rifampicin and it is difficult and expensive to treat (Weyer, 2005). The cure rate of MDR-TB is currently less than 50% and it is therefore essential to prevent its development. MDR-TB is the consequence of human error in prescription of chemotherapy, management of drug supply, patient management and patient compliance.

Health care workers can reduce the threat of MDR by prescribing the correct TB drugs in the correct dose for new TB patients, ensure that the patients adhere to treatment through DOTS and promptly detect and investigate any TB patient who fails to respond to TB drugs (DOH, 2000). Patients with active, untreated MDR-TB can infect large numbers of HIV-positive individuals, leading to outbreaks of MDR-TB with high case-fatality rates. It is therefore important that MDR-TB be prevented by rigorous adherence to the principles of the TB Control Programme (the DOTS strategy) and by patiently and consistently building partnerships with patients, their families and communities to cure tuberculosis at the first attempt (Weyer, 2005). Since the mid-eighties, patients with MDR-TB have been diagnosed in each of the nine provinces in South Africa, and a recent national survey by the Medical Research Council indicated a rate of 1.6% MDR in new TB cases and 6.6% in previously treated cases. This translates into at least 6 000 new cases of MDR-TB in South Africa each year (DOH, 2004). For this reason the DOTS-Plus strategy (which is an integrated approach to the management of TB and MDR-TB) was implemented in South Africa for the management of MDR-TB.

Nosocomially acquired MDR-TB presented a serious public health problem in the early 1990s initially in the United States of America and then in the Southern European countries (Davidsons, 2002). MDR-TB is at critical levels in specific regions of the world and limited to localised epidemics. DOTS has been adopted to prevent the generation of resistant strains and to carefully introduce second-line drugs to treat patients with MDR (Espinal, 2003). XDR-TB has emerged recently as a serious threat to TB control. XDR-TB is resistant to isoniazid, rifampin and any fluoroquinolone and at least one of three injectable second-line drugs (amikacin, kanamycin or capreomycin) (Mori, 2007). Several factors are implicated in the increased risk of individuals developing TB. Patient related factors are age (children more than young adults), first-generation immigrants from high prevalence countries, close contact of patients with smear – positive pulmonary TB, chest radiograph evidence of self-healed TB and primary infection less than one year previously. Associated diseases that increase the risk of TB are HIV, silicosis, immuno-compromised states, malignancy (especially lymphoma and leukaemia), Type 1 diabetes mellitus, chronic renal failure and gastrointestinal disease associated with malnutrition (Davidsons, 2002).

2.3 AETIOLOGY

TB is a highly infectious, debilitating disease that commonly involves the pulmonary system, lymph nodes, soft tissue or skin including the mouth (Davidsons, 2002; Randy *et al*. 1993). The genus *Mycobacterium* contains a variety of species, ranging from human pathogens to relatively harmless organisms. As a major cause of TB, *M. tuberculosis is* by far the most historically prominent member of this group of bacteria. The subtypes of *Mycobacteria* involved in infections of the head and neck are divided into two major categories: *M. tuberculosis* and atypical *Mycobacteria.*
The atypical are opportunistic and usually cause infection in patients with weak immunologic defences, such as young children and immuno-compromised patients (Munck and Mandpe, 2003). In addition to their very slow growth on special enriched media, these aerobic slender rods are characterised by their acid-fast staining features. The unusually high lipid content of the cell wall confers the organisms with the ability to strongly retain the red dye (carbolfuchsin) after treatment with an acid-alcohol solution. This unique structure also allows the bacteria to survive outside a host's body, suspended in airborne micro droplet nuclei for extended periods of time.

Contrary to myth, *M. tuberculosis* is not a highly contagious bacterium. It does not synthesise potent exotoxins or extra cellular enzymes, and it is not surrounded by an antiphagocytic capsule. Onset of infection appears to be related to the ability of the tubercle bacilli to multiply within the host cells and tissues while at the same time resisting host defences. Infection with *M. tuberculosis* typically requires prolonged close contact of a susceptible host with an infectious source. The closeness of contact with aerosol bacilli and the degree of infectivity of the mycobacterial source are the most important considerations for infection (Davidsons, 2002).

The overwhelming majority of primary human infection involves the inhalation of mycobacteria-laden respiratory micro-droplets (CDC, 1994; Bates and Stead, 1993). When a person has active pulmonary TB (the most common form of TB) they cough up very small infectious particles that can remain in the air for long periods. These particles, called "droplet nuclei", when inhaled, can establish an infection in the lungs. The diameter of the aerosol droplets range from 1 to 5 microns. Dispersal of *M. tuberculosis* occurs via these droplets as a result of coughing, sneezing or even

speaking. Micro-droplet nuclei are small enough to bypass protective host bronchial mucocilliary defences, leading to mycobacteria subsequently replicating in both free alveolar spaces and within phagocytic cells.

Repeated prolonged exposure to air that has been contaminated by the droplets from a person with TB predisposes others to infection. People living in the same home as an infected individual, or close friends or co-workers, who routinely breathe the same mycobacteria-contaminated air from an undiagnosed or untreated person with pulmonary TB, have a high risk of acquiring TB (Davidsons, 2002).

Transmission is most common indoors in overcrowded and poor housing conditions since direct sunlight can kill these infectious particles. A person's risk of exposure is determined by the concentration of droplet nuclei in the air and the length of time a person is exposed to the air. TB can occur in areas other than the lungs, such as in the lymph nodes, central nervous system, and the gastro-intestinal tract. This is referred to as extra-pulmonary TB and is most common in HIV positive people, infants and children (Achmat and Roberts, 2005). Extra-pulmonary TB, which is rarely infectious, has dramatically increased. It occurs in 15% of all patients with TB and in 70% of patients with AIDS and TB.

Extra-pulmonary TB represents a diagnostic challenge and is usually diagnosed by specialists in the involved anatomic area (Goguen and Karmody, 1995). Onset of clinical disease is characterised by gradual infiltration of neutrophils, macrophages and T lymphocytes. Distinctive granulomatous TB lesions called tubercles may appear anywhere in the lung parenchyma; however, they are most evident in the periphery. The immunocompetence of the affected host plays a significant role in controlling the extent and severity of resultant disease (Ellner, 1997; Orme *et al*. 1993). Most people infected with *M. tuberculosis* develop a positive type IV hypersensitive skin test reaction. Once infected with the bacteria, it remains dormant for many years (latent TB) because a properly working immune system is capable of suppressing the infection and preventing the bacteria from multiplying. When the immune system is weakened for example by HIV or poor nutrition, the bacteria begin to multiply and this often leads to active TB. The vast majority (90%) of HIV negative people infected with *M. tuberculosis* never develop TB. For those infected

individuals who develop clinical symptoms, fatigue, malaise, weight loss, night sweats and fever are common signs, in addition to positive chest radiographic manifestations.

2.4 PATHOLOGY AND PATHOGENESIS

Initial mycobacterial infection may progress to several different states depending on the extent of *M. tuberculosis* exposure and resistance of the patient. These include (i) asymptomatic primary tuberculosis, (ii) symptomatic primary tuberculosis, (iii) progressive primary tuberculosis and (iv) re-activation tuberculosis (Davidsons, 2002).

A major risk factor for the progression of initial infection with tubercle bacilli to more severe disease stages is the absence of an adequate host acquired cellular immune response to mycobacterial antigens. The ability of an infected individual to develop dual cellular and humoral immune responses against *M. tuberculosis* antigens thus greatly influences disease onset and progression.

Asymptomatic primary tuberculosis: Individuals may be infected with *M. tuberculosis* without apparent clinical manifestations. When the skin is tested, individuals with asymptomatic primary tuberculosis display a positive tuberculin test reaction indicating that they have been infected and have developed cell-mediated immunity against the bacteria. This protective immune response prevents the continued multiplication and dissemination of the bacteria, but it does not destroy all of the bacteria present. The remaining bacteria are sequestered within the tubercles in the affected tissues and may be the source of bacteria that initiate reactivation tuberculosis (Davidsons, 2002).

Symptomatic primary tuberculosis: In symptomatic primary tuberculosis, *M. tuberculosis* is spread via the lymphatics, to cause granulomatous inflammation in the lung periphery and hilar nodes, and is accompanied by respiratory symptoms. The tonsil, intestine or skin may also be the site of primary disease (Davidsons, 2002).

A small sub pleural lesion (the Ghon focus) develops following inhalation with *M. tuberculosis*. Bacilli are rapidly transported to the regional (hilar) lymph nodes and the primary complex develops. Activated macrophages that have ingested the bacilli aggregate and the lesions enlarge. Two T cell-mediated immune responses start at 2-4 weeks. The non-activated macrophages containing bacilli are destroyed by a delayed-type hypersensitivity reaction which also results in tissue necrosis and caseation. Macrophages are activated into epitheloid cells with formation of granulomas at the periphery of the caseation. The primary complex heals spontaneously in 1-2 months in 85-90% of cases and the tuberculin skin test becomes positive (Davidsons, 2002).

Progressive primary tuberculosis: A much more serious disease may develop in those individuals who are less resistant to the tubercle bacilli. Multiplication of *M. tuberculosis* is not contained in 10-15% of cases and lymph node enlargement results in either local pressure effects, lymphatic spread to the pleura or pericardium, or rupture into an adjacent bronchus or pulmonary blood vessel. Micro-organisms may spread throughout the body either (i) by means of the blood resulting in miliary tuberculosis, (ii) via the respiratory tissues, inducing bronchopneumonia or (iii) throughout the gastro-intestinal tract as a result of organisms being coughed up and swallowed (Davidsons, 2002). In miliary tuberculosis, foci of infection occur in distant organs and tissues but most frequently develop in the meninges, lungs, liver and renal cortex. Although cell-mediated immunity may develop in some patients, others may not react (anergy) when the skin is tested with tuberculin protein preparations. Anergic patients have a poor prognosis for recovery and often die without rapid treatment (Davidsons, 2002).

Reactivation tuberculosis: Reactivation tuberculosis occurs in individuals who have developed primary tuberculosis and who are asymptomatic, but who still carry the bacteria within tubercles. Of these patients, 5-10% reactivates during their lifetime resulting in post primary diseases, which are predominantly pulmonary (75%) and infectious (50% smear-positive). Reactivation of disease is thought to be due to the activation of persistent bacteria in the tubercles of previous infection that become activated by some alteration in host resistance (Davidsons, 2002).

Infection is characterised by tubercle formation, caseation, fibrosis and further extension of the lesion. Progression may advance into a bronchus, leading to cavitation of the lung and secretion of infectious sputum. Infection after exposure, development of progressive primary disease and re-infection from other infectious cases are all increased in HIV-infected individuals. In the presence of good immune function in HIV patients, clinical disease resembles classical post-primary TB. In patients where significant immunodeficiency has occurred, the presentation is either disseminated or extra-pulmonary. There are reduced smear-positive rates in pulmonary TB, less cavitation, atypical chest radiograph, increased disseminated disease, more extra-pulmonary infection and greater risk of adverse drug reactions in HIV patients (Davidsons, 2002).

2.5 CLINICAL FEATURES OF PULMONARY DISEASE

Primary pulmonary TB usually occurs in childhood and is generally asymptomatic – patients may develop a febrile illness. Erythema nodosum may present with primary TB and is associated with a positive tuberculin skin test. Progressive primary disease may appear during the course of the initial illness or after a latent interval of weeks or months. Features depend on the site affected.

Miliary TB is a severe infection that is often diagnosed late. It may start suddenly or there may be a period of 2-3 weeks when fever, night sweats, anorexia, weight loss and a dry cough are present. A headache may indicate co-existence with TB meningitis. Lesions (resembling millet seeds) are found throughout the lungs and anaemia and leucopenia may be present.

Post-primary pulmonary TB in adults is a sub-acute illness characterised by cough, haemoptysis, dyspnoea, anorexia and weight loss associated with fevers and night sweats. Earliest radiological change is an ill-defined opacity situated in one of the upper lobes. Two or more areas of the lung may be involved and it may be bilateral. As the disease progresses, consolidation, collapse and cavitation develop. Collapse may be marked in extensive disease and this could result in displacement of the trachea and mediastinum. Draining of a caseous lymph node into an adjoining bronchus may result in tuberculous pneumonia (Davidsons, 2002).

2.6 CLINICAL FEATURES OF EXTRA-PULMONARY DISEASE

Lymph nodes are the most common extra-pulmonary site of disease. The most frequently affected glands are the cervical and the mediastinal followed by the axillary and inguinal. The nodes are initially mobile and painless and then become matted. With caseation and liquefaction, the swelling becomes fluctuant and may discharge through the skin with the formation of a "collar-stud" abscess and sinus formation. Fevers and night sweats are not frequently present and the tuberculin skin test is usually positive. Enlargement, development of new nodes and suppuration may occur during or after treatment without evidence of continued infection and surgical excision is rarely necessary (Davidsons, 2002).

Gastrointestinal TB patients present with a wide range of signs and symptoms. Upper tract involvement is rare. Prominent features include fever, night sweats, anorexia and weight loss. *Pericardial disease* occurs in two main forms – pericardial effusion and constrictive pericarditis. Presentation is usually insidious (Davidsons, 2002).

Meningeal disease is the most important form of *Central nervous system* disease. This can be life-threatening and fatal if not diagnosed early. *TB of the spine* involves the lower thoracic and lumbar spine and usually presents with chronic back pain. TB can affect any joint, but most frequently involves the hip or knee. Pain and swelling is usually present and fever and night sweats are uncommon. Reduction in joint space and erosions appear as the disease progresses.

In *Genitourinary* disease patients are mildly symptomatic for many years. Haematuria, frequency and dysuria are often present (Davidsons, 2002).

2.7 HEAD AND NECK MANIFESTATIONS OF TB

Head and neck TB can present in many forms depending on the site of involvement, the stage of the disease and the immune status of the patient (Al-Serhani, 2001). Head and neck TB forms nearly 10% of all extra-pulmonary manifestations of the disease.

Extra-pulmonary presentations form a major proportion of new cases, especially since the advent of the AIDS epidemic. Therefore oral health professionals need to be aware of TB in the head and neck region and its varied manifestations (Prasad *et al*. 2007). The cervical lymph nodes are one of the commonest sites of extra-pulmonary TB. Other sites include the oral cavity, nose, ears, larynx, pharynx, thyroid, salivary glands, eye, cervical spine and mandible (Menon *et al*. 2007).

2.7.1 Cervical Lymph Nodes

The cervical lymph nodes are the most common site in the head and neck region to be affected by TB (Nohrstrom *et al*. 2007; Prasad *et al*. 2007; Munck and Mandpe, 2003). The presentation could be an isolated, discreet, affected node or the more common collection of matted nodes (Munck and Mandpe, 2003). The upper deep cervical nodes are commonly involved with matting, ulceration and abscess formation (Prasad *et al*. 2007). A fluctuant mass is present in 10% of patients and a draining sinus is present in 5% of patients. Skin overlying the lesion may appear erythemic and may be tender to palpation. The clinical course and treatment are different for tuberculous and non-tuberculous mycobacteria, therefore it is important to differentiate between masses caused by them. The posterior and supraclavicular lymph nodes are involved with tuberculous mycobacterial infections. Nontuberculous mycobacterial infections involve submandibular and submental cervical lymph node groups. These infections are generally seen in children between the ages of 1 and 5 and in immunocompromised patients. Constitutional symptoms are rare and chest x-rays are negative for signs of pulmonary TB (Munck and Mandpe, 2003).

The incidence of tonsillar, submandibular and submental lymph nodes affected by *M. tuberculosis* could be as high as 10% of cases of pulmonary TB. The consistency of nodules varies with the stage of disease. A clinical classification by Hooper states that in Stage 1 the nodes are enlarged, firm, mobile, discrete and slightly tender showing non-specific reactive hyperplasia. In Stage 2 the nodes are larger, rubbery and fixed to surrounding tissues because of periadenitis with caseation. In Stage 3 there is central abscess formation, Stage 4 collar-stud abscess formation and Stage 5 sinus formation (Ishikawa *et al*. 1982).

Treatment in the management of peripheral node TB includes surgical incision with chemotherapy, chemotherapy first and then surgery or chemotherapy alone with anti-tubercular drugs for varying durations (Williams and Jones, 1995; Subrahmanyam, 1993).

2.7.2 Larynx

There are two theories that attempt to explain the infectious route of laryngeal TB. The bronchogenic theory states that the larynx is infected by direct spread of large numbers of bacilli from the endobronchial tree while the hematogenous theory suggests that the larynx becomes involved through the hematogenous route from other distant primaries rather than direct spread from the airway.

The bronchogenic mode of transmission is more common therefore a chest x-ray examination should be emphasized (Wang *et al*. 2009; Wang *et al*. 2007). Laryngeal TB is rare occurring in less than 1% of TB cases. Hoarseness is the most common symptom. Patients may also describe odynophagia, dysphagia, cough, otalgia and signs of stridor (Wang *et al*. 2009; Wang *et al*. 2007; Lim *et al*. 2006; Nalini and Vinayak, 2006; Munck and Mandpe, 2003; Rinaggio, 2003; Yencha *et al*. 2000; Kandiloros *et al*. 1997; Williams and Jones, 1995; Rupa and Bhanu, 1989; Levenson *et al*. 1984). The vocal folds (true followed by the false) are the most common site and make up 50-70%, closely followed by the ventricular bands, which make up 40-50% of cases. The epiglottis, aryepiglottic fold, arytenoid, posterior commissure and subglottis make up 10-15% of cases. The anterior half of the larynx is affected twice as often as the posterior half (Williams and Jones, 1995).

Clinical features in laryngeal TB vary from ulcers on the true vocal folds to hypertrophic nodules and hyperaemia and oedema of the arythenoids and aryepiglottic folds. Broad based exophytic lesions without significant erythema and oedema may also be seen (Prasad *et al*. 2007; Lim *et al*. 2006; Yencha *et al*. 2000; Levenson *et al*. 1984). Histopathological examination must be done to differentiate between cancer and laryngeal TB (Munck and Mandpe, 2003; Yencha *et al*. 2000; Williams and Jones. 1995). Patients with laryngeal TB are treated with anti-tuberculin medications

and demonstrate a quick clinical response and rarely require a tracheotomy to secure the airway (Munck and Mandpe, 2003; Williams and Jones, 1995).

2.7.3 Nasal

Nasal TB is rare. The English literature has reported 26 cases during the twentieth century. It is caused either by a primary infection or pulmonary disease (Goguen and Karmody, 1995). Rarity is the result of the nasal mucosa being resistant to the *M. tuberculosis*. Common sites of involvement are the cartilaginous septum and the inferior turbinate. The lesions may present as ulcerated, infiltrative or polypoidal. The lesions of the paranasal sinuses present as pale, polypoidal mucosa of the maxillary anthrum or multiple polyps of the ethmoid. Bone involvement with fistula formation is rare (Prasad *et al*. 2007; Williams and Jones, 1995). TB of the nasal cavity is painless and causes nasal obstruction and catarrh (Williams and Jones, 1995). Treatment for nasal TB is varied. Surgical excision, diathermy, cautery, lactic acid application and radium treatments were the early regimens. There could be recurrence with surgical excision. Since 1951 reported cases have been treated with anti-TB medications and no recurrences have occurred (Goguen and Karmody, 1995).

2.7.4 Oral Cavity

Less than 3% of the cases involve the oral cavity (Molinari and Chandrasekar, 1991; Mani, 1985). The bacteria can infect oral tissues and lymph nodes. Within the oral cavity, lesions occur in the soft tissues and supporting bone and in tooth extraction sites, and the tongue and floor of the mouth. They occur in the following order – tongue tip, tongue border and floor of the mouth, soft palate anterior tonsillar pillar and uvula and dorsum and base of the tongue. Oral lesions appear as painful ulcers, nodules, fissures and tuberculosis granulomas (Tovaru *et al*. 2008; Prasad *et al*. 2007; Ajay *et al*. 2006; Feller *et al*, 2005; Miziara, 2005; Rinaggio, 2003; Von Arx and Husain, 2001; Eng *et al*. 1996; Dimitrakopoulos *et al*. 1991; Hashimoto and Tanioka, 1989; Waldman, 1982; Prabhu *et al*. 1978; Rauch and Friedman, 1978). The tuberculosis oral ulcerations may be solitary or multiple, occasionally painful and usually involves the dorsum of the tongue. The mature ulcer has an irregular outline

and a rough or granular surface. The surrounding mucosa is erythematous and oedematous.

The infection in the oral cavity requires mucosal injury and could result from pulmonary disease. The gingival, dental sockets and buccal folds are commonly involved by direct inoculation. These lesions can be distinguished from carcinoma by histological examination (Tovaru *et al*. 2008; Ajay *et al*. 2006; Feller *et al*, 2005; Miziara, 2005; Munck and Mandpe, 2003; Von Arx and Husain, 2001; Eng *et al*. 1996; Williams and Jones, 1995; Hashimoto and Tanioka, 1989; Verma *et al*. 1989; Waldman, 1982; Prabhu *et al*. 1978; Rauch and Friedman, 1978; Brennan and Vrabec, 1970).

Primary tuberculosis lesions of the mouth which are seen in younger patients are generally painless and there may be regional lymphadenopathy present. When they become secondarily infected with bacteria from the oral cavity, they may become painful. Secondary TB is more common among older patients and is usually a complication of pulmonary disease (Tovaru *et al*. 2008; Miziara, 2005; Iype *et al*. 2001; Hashimoto and Tanioka, 1989; Mani, 1985; Waldman, 1982). Tongue lesions are usually painful, grayish yellow, firm and well demarcated. Gingivitis tuberculous presents as irregular, nodular lesions that may cause more diffuse involvement (Ajay *et al*. 2006; Iype *et al*. 2001; Waldman, 1982).

TB of the oral cavity has become a forgotten diagnosis of oral lesions because of its rarity. With the recent reversal in the incidence of TB it should always be included in the differential diagnosis of oral ulcerations as a delay in the diagnosis may have serious consequences (Tovaru *et al*. 2008; Ajay *et al*. 2006; Von Arx and Husain, 2001). Chemotherapy is used to treat TB of the oral cavity (Williams and Jones, 1995).

2.7.5 Jaws

TB of the mandible and tempro-mandibular joint (TMJ) is rare. The incidence does not exceed 1.4% of all patients affected by the disease. Young patients with pulmonary involvement can present with TB of the mandible. TMJ TB can be a

primary infection or a fistulous communication from TB otitis media. Trismus and a painful fluctuant swelling in front of the ear are the symptoms experienced (Prasad *et al*. 2007).

TB of the jaws is manifested as a tuberculous granuloma or tuberculous osteomyelitis. Radiographically the tuberculous granuloma presents as a periapical radiolucency involving a nonvital tooth. Pain and swelling of the affected area is present. The swelling later softens and ruptures intra-orally or extra-orally. Sinus tracts are then present and trismus occurs when the mandible is affected (Mavropoulou and Yannoulopoulos, 1986). The spread of infection may occur through an extraction socket, mucosal tear associated with an erupting tooth, regional extension of a soft tissue lesion to underlying bone, or by haematogeneous spread. Apical osteitis, periodontitis with horizontal bone loss or a widespread destructive osteolytic lesion are some of the presentations. It may be mistaken for a dental abscess in the absence of systemic symptoms (Bhatt and Jayakrishnan, 2001). Patient recovers with anti-tuberculous treatment. In tuberculous osteomyelitis complete drainage of the abscess and removal of necrotic bone is done in combination with anti-tuberculous chemotherapy. Although TB rarely affects the jaws, it should be considered in differential diagnosis of chronic joint disease since this disease continues to be a health problem in both developed and underdeveloped countries (Dinkar and Prabhudessai, 2008; Soman and Davies, 2003; Bhatt and Jayakrishnan, 2001; Mavropoulou and Yannoulopoulos, 1986).

2.7.6 Cervical Spine

TB of the cervical spine occurs more often in prepubertal children than in adults. The commonest symptom of TB cervical spine is pain followed by dysphagia, dyspnoea and stridor due to pressure effects. Abscess formation presents as a retropharyngeal abscess, sternomastoid abscess or parotid mass (Prasad *et al*. 2007; Williams and Jones, 1995). Surgery is performed on large abscesses (Williams and Jones, 1995).

2.7.7 Aural

TB affecting the middle ear cleft has dramatically decreased over the past forty to fifty years. This could be due to the availability of specific bactericidal anti-

tuberculous drugs, improvement in the public health services, massive inoculation of cattle with the virtual eradication of Bovine-strain TB, improvement in housing and widespread Bacille Calmette-Guérin (BCG) inoculation campaigns directed at babies and children of school age (Ramages and Gertler, 1985).

Aural TB is usually found in children and young adults. Typical features are painless otorrhoea, central perforation, pale middle-ear granulations, severe hearing loss and facial paralysis. Bone necrosis and sequestration in the mastoid is commonly found. With superimposed infection there may be otalgia, foul-smelling infection, acute mastoid infection and fistulisation (Prasad *et al*. 2007; Vaamonde *et al*. 2004; Munck and Mandpe, 2003; Lee and Schecter, 1995; Williams and Jones, 1995; Yaniv, 1987; Ramages and Gertler, 1985). Multidrug therapy is the treatment of choice while awaiting culture and sensitivity results for more targeted therapy. Surgical intervention is carried out on patients with facial paralysis, subperiosteal abscess formation, fistulisation, labyrinthitis, intracranial complications and progressive disease recalcitrant to medical therapy (Munck and Mandpe, 2003; Williams and Jones, 1995; Ramages and Gertler, 1985).

TB osteomastoiditis is a rare complication of TB today. When it occurs it may cause significant morbidity. Diagnosis is difficult if the patient shows no other manifestations of the disease and may be delayed for months or years, since most physicians are not familiar with the typical presenting features (Pavlopoulou *et al*. 2000).

2.7.8 Salivary Glands

TB of the salivary glands is rare and only about a hundred cases have been reported in the world wide literature. It can be central, with involvement of the inter-glandular lymph nodes, or diffuse, with involvement of the parenchyma. Parotid involvement presents as a firm, non-tender mass. Abscess formation and fistulisation may also occur. Seventh nerve palsy is rarely seen (Prasad *et al*. 2007). The parotid gland is the most commonly involved followed by the submandibular and then sublingual gland. In the parotid the infection arises in the intra-parotid lymph nodes the bacilli reaching the gland either via the duct or through the lymphatic channels.

Patients are generally well with no evidence of pulmonary involvement therefore TB infection is often indistinguishable from neoplasm. Pain manifests later and facial palsy is rare (Williams and Jones, 1995). Anti-tuberculosis chemotherapy is the standard treatment. Surgical intervention is avoided in these patients (Munck and Mandpe, 2003; Williams and Jones, 1995). TB of the salivary gland should always be included in the differential diagnosis of salivary gland tumour especially in the areas where TB is endemic. This would avoid unnecessary surgery for histological confirmation and anti-tuberculous medication would be sufficient to resolve the condition. Therefore the combination of fine needle aspiration cytology and molecular biology methods such as polymerase chain reaction should be used as initial diagnostic tools for the diagnosis of salivary gland TB (Kim *et al*. 2005).

2.7.9 Pharynx

Pharyngeal infection is slowly progressive and presents as a chronic nodular irregularity of mucosal surfaces. The two main sites of pharyngeal involvement are the nasopharynx and oropharynx. These are mostly primary infections. Nasal obstruction with rhinorrhea is the most common complaint. Cervical lymphadenopathy may accompany nasopharyngeal TB. Ulcerations and fibrosis of the tonsils make it difficult to distinguish between tonsillar TB and tonsillar carcinoma (Munck and Mandpe, 2003; Williams and Jones, 1995). Treatment with chemotherapy shows rapid improvement (Williams and Jones, 1995).

2.7.10 Eye

TB of the eye is rare and is found in about 1.4% of hospitalized patients. The common site of occurrence is the posterior and anterior uveal tract. Primary or secondary involvement of the eye can occur. Primary disease is the result of direct inoculation by contaminated fingers, dust or droplet nuclei from sputum and is rare. This results in conjunctivitis, corneal ulcerations or abscess formation. The causative organism could be *M. tuberculosis* or *M. fortuitum*. In secondary TB infection of the eye the organism reaches the eye via the blood and this may be the only manifestation of the disease (Waldman, 1982).

2.8 DIFFERENTIAL DIAGNOSIS

A differential diagnosis for oral TB should include malignancy, traumatic and aphthous ulcers, syphilis, sarcoidosis and deep mycotic infections (Von Arx and Husain, 2001; Eng *et al*. 1996; Dimitrakopoulos *et al*. 1991; Hashimoto and Tanioka, 1989; Rauch and Friedman, 1978; Brennan and Vrabec, 1970). Differential diagnosis for TB of the jaw is non-specific inflammation, actinomycosis, neoplastic lesions or osteogenic sarcoma (Mavropoulou and Yannoulopoulos, 1986) and lymphoma or secondary metastasis in the neck (Al-Serhani, 2001).

2.9 DIAGNOSIS

Table 1: Patient history prompting suspicion of active TB

1	Productive cough (>3 weeks) – pulmonary TB
2	Other symptoms (fever, chills, night sweats, fatigue, chest pain, loss of appetite and weight, weakness, coughing up blood)
3	Extra-pulmonary TB (occurs in 15% of cases)
4	Patients with TB and HIV infection – 40-75% have extra-pulmonary TB and pulmonary TB
5	History of TB exposure and/or previous TB infection (active TB)

Source: Davidsons (2002): 528

A diagnosis of infection with *M. tuberculosis* relies on (i) development of a positive delayed hypersensitivity (tuberculin) skin reaction to purified protein derivative (PPD), a mycobacterial antigen isolated from bacterial cultures and (ii) demonstration of acid-fast mycobacteria in clinical specimens. Information obtained while collecting a patient's medical history can provide evidence of suspicion of TB (Table 1) (Davidsons, 2002).

The tuberculin skin test measures the body's immune response to an injection of tuberculin PPD. The Mantoux test injects a known amount of PPD between the layers of skin (intra-dermally). The reaction to the test at the site of injection is measured 48-72 hours later. A positive test indicates infection with TB, but not

necessarily TB disease. A negative tuberculin skin test does not exclude TB. The tuberculin skin test is a low sensitivity or specificity test which is useful only in primary or deep-seated infections.

If the chest X-ray is typical of TB and the skin test is negative, TB can be diagnosed. Conditions which may suppress the tuberculin skin test and give a false negative result include: HIV infection, malnutrition, severe viral infections (eg. measles, chicken pox), cancer, immunosuppressive drugs (eg. steroids) and severe disseminated TB (Randy *et al*. 1993).

Direct microscopy of samples (Ziehl-Neelsen or auramine staining) and culture can confirm mycobacterial infection. The BACTEC system (automated detection system for mycobacteria) is used to obtain drug susceptibility profiles. Molecular methods which allow the detection of rifampicin resistance (a marker for MDR) is used when MDR-TB is suspected. Diagnosis of TB using specimens includes the following: For respiratory – Sputum, gastric washing, bronchoalveolar lavage and transbronchial biopsy and for non-respiratory – fluid examination and tissue biopsy. Diagnosis of TB using diagnostic tests include circumstantial (ESR, C-reactive protein, anaemia), tuberculin skin test, stains, nucleic acid amplification, culture and response to empirical antituberculous drugs. Tuberculin skin testing uses the Heaf or Mantoux technique (Davidsons, 2002).

Examination of oral tissues using acid-fast staining methods may produce negative results due to a paucity of bacilli in oral lesions. This method does not differentiate between the various types of mycobacteria. Biopsy of the lymph nodes using fine needle aspiration and the acid-fast staining and culture methods can achieve a definitive diagnosis without open biopsy. Pulmonary TB even in those patients without systemic signs and symptoms is ruled out by chest radiographs. In cases of negative sputum smears, pulmonary TB is confirmed using acid-fast smear and culture of laryngeal swabs. PPD tests should be done routinely, although the BCG vaccination may produce a positive reaction. Immuno-compromised patients may produce false-negative results (Bhatt and Jayakrishnan, 2001).

2.10 RISK FACTORS

The re-emergence of *M. tuberculosis* as a significant public health problem in South Africa appears to be the result of a combination of changing host susceptibility factors and declining social conditions. The most frequent risk factor is infection with HIV (Small *et al.* 1991; Barnes *et al.* 1991; Theuer *et al*. 1990; Reider *et al*. 1989; Selwyn *et al*. 1989). The suppressive effect of HIV infection on cell-mediated immunity increases host susceptibility to a variety of microbial pathogens that are normally controlled by these defence mechanisms.

Table 2: Risk factors associated with TB

1	Known or suspected HIV infection
2	Persons with close contacts with infectious persons – exposure to a pulmonary TB case, especially a sputum smear-positive case
3	Persons with medical conditions that increase the risk of contracting HIV
4	Intravenous drug abusers
5	Persons from low socio-economic groups
6	**Malnutrition**: Marasmus Kwashiorkor in children Chronic alcohol abuse which is associated with malnutrition Poor nutrition in any individual
7	**Medications:** Long term cortisone therapy Chemotherapy for malignancies or transplants
8	**Stress:** Mental or physical stress can cause suppression of the immune system
9	Prisoners
10	Industrial silica dust exposure (eg. In underground miners)

Source: Davidsons (2002): 529

2.11 TREATMENT, CONTROL AND PREVENTION

Prior to the advent of antimicrobial chemotherapy, approximately 50% of people with active TB died within two years after the onset of symptoms (Styblo, 1980). Regimens of multiple antibiotics are currently used to treat patients with active TB to ensure tissue penetration and minimise emergence of resistant organisms.

General guidelines for appropriate chemotherapy include the necessity for long-term treatment intervals, initiation of treatment if sputum smear is positive for acid-fast bacilli and patient compliance (a major factor in determining chemotherapy success) (Davidsons, 2002).

The key factor in the principles of treatment to stop the spread of TB in a community is to start treating patients who are coughing up living bacilli as soon as possible. It is crucial that correct drugs are given for the correct period of time for treatment to be effective. It must be established whether the patient is a new patient (has never been treated for TB before) or a retreatment patient (treated for more than four weeks at any time in the past). Treatment with a combination of drugs is the best. Patients must take the treatment for five days a week. No trials of therapy should be given as this is one of the reasons for an increase in drug resistance (DOH, 2000).

The three main properties of the essential anti-TB drugs are bactericidal, sterilizing and the ability to prevent resistance. Isoniazid and Rifampicin are the most powerful bactericidal drugs, active against all populations of TB bacilli. Pyrazinamide and streptomycin are bactericidal against certain populations of TB bacilli. Pyrazinamide is active in an acid environment against TB bacilli inside macrophages. Streptomycin is active against rapidly multiplying extracellular bacilli and Ethambutol is bacteriostatic (DOH, 2000). If the patient is an irregular attendee in the intensive phase of treatment (more than 10 missed doses), the standardized re-treatment regimen must be started. If more than two months in the continuation phase of treatment is missed, the continuation phase must be completed if the sputum smear is negative and retreatment must begin if the sputum is smear positive. Retreatment patients should be hospitalized for the initial two months as they are more likely to develop MDR (DOH, 2000).

The DOTS strategy, which is the only globally recognised strategy for effective TB control, ensures that infectious TB patients are identified and cured using standardized drug combinations. Patients are observed by treatment supporters as they swallow their drugs daily. The treatment supporter can be a responsible member of the community, employers or colleagues. The person should know the signs and symptoms of TB, side effects of TB drugs and the importance of regular intake of TB medication.

The DOTS strategy is the most effective strategy available for controlling TB. It was adopted by the South African National Department of Health after it was realized that their TB control efforts had been ineffective. The five key elements of the DOTS strategy are outlined in Table 3 (DOH, 2000).

Table 3: DOTS Strategy

1	Government commitment to sustained TB control activities.
2	Sputum smear microscopy to detect the infectious cases among those people attending health care facilities with symptoms of TB, most importantly cough of three week's duration or more.
3	Standardized short-course anti- TB treatment for at least all confirmed sputum smear positive pulmonary TB cases, with direct observation of treatment for at least the initial two months.
4	A regular, uninterrupted supply of all essential anti-TB drugs.
5	A standardized recording and reporting system which allows assessment of treatment results and overall programme performance.

Source: DOH (2000): 9

The priority of DOTS is to cure infectious patients and its core elements are outlined in Table 4 (DOH, 2000).

Table 4: Core Elements of DOTS

1	Sustained TB control activities
2	Sputum smear microscopy to detect the infectious cases among those people attending health care facilities with symptoms of TB, most importantly cough of three week's duration.
3	Standardized short-course anti-TB treatment with direct observation.
4	An uninterrupted supply of TB drugs.
5	A standardized recording and reporting system which allows assessment of treatment results.

Source: DOH (2000): 5

The DOTS strategy is effective in treating TB but may be insufficient in treating MDR-TB therefore the DOTS-plus programme was implemented for the treatment of

MDR-TB patients. DOTS-plus involves the use of second-line anti-tuberculosis drugs which are more toxic and expensive and less effective than first-line drugs.

The regimen includes two or more drugs to which the isolate is susceptible, including one drug given parenterally for more than six months. The total duration of treatment is 18-24 months and treatment is directly observed. Optimal use of the DOTS-plus programme can lower mortality caused by TB and MDR-TB (Sterling *et al*. 2003).

In South Africa the standardised approach to DOTS-plus comprises of treatment at dedicated MDR-TB referral facilities where patients are admitted for four months of therapy or until sputum conversion, specialised teams overseeing all aspects of MDR-TB management, patients being regularly monitored and documented (patients registered on the DOTS-plus Electronic Register at the MDR-TR referral centres) and ambulatory treatment after discharge provided DOT is ensured and patient follows up for five years after treatment completion at six monthly intervals (Weyer, 2005).

BCG, an attenuated strain of *Mycobacterium bovis*, has been used for more than 80 years to protect humans against TB and is up to 80% protective in 10-15 year olds, but less so in adults. It is recommended for those that do not respond to tuberculin. Those that respond to tuberculin skin tests should be referred for clinical and radiological examinations.

TB is the most significant cause of mortality in people living with HIV in developing countries therefore good treatment outcomes is critical to decrease HIV-related morbidity and mortality. A combination of cure and completion rates results in treatment success. High default and loss to follow up rates could be improved through strengthened DOT and community adherence programmes. Community workers assist by confirming addresses, educating patients about the importance of good adherence, encouraging patients to go to health facilities for sputum smear examinations at the end of the intensive and continuation phases and tracing defaulters. The critical challenges to effective TB control are highlighted in Table 5 (Grimwood *et al*. 2006).

Table 5: Critical challenges to effective TB control in South Africa

1	Poor financial and human resources support to the TB programme.
2	Poor support of the TB programme especially at provincial level
3	Poor management of patients which leads to patients defaulting from treatment
4	High mobility of patients especially in the urban areas and poor referral systems
5	Late detection of patients
6	Inaccessible and of questionable quality laboratory services
7	Lack of knowledge of TB and the importance of completing treatment
8	Poverty
9	Co-infection of patients with TB and HIV

Source: Adapted from Grimwood *et al.* (2006): 82

2.12 CHEMOTHERAPY

Chemoprophylaxis is administered to prevent infection progressing to clinical disease and is recommended for under 16 year olds with strongly positive Heaf tests, under 2 year olds in close contact with smear-positive pulmonary disease, those in whom recent tuberculin conversion has been confirmed, and babies of mothers with pulmonary TB. It should also be considered for HIV-infected close contacts of a patient with smear-positive disease. Rifampicin and isoniazid for 3 months, rifampicin and pyrazinamide for 2 months, or isoniazid for 6 months are all effective.

Short-course therapy consists of 2 months with 4 drugs (rifampicin, isoniazid, pyrazinamide and either ethambutol or streptomycin) followed by 4 months of rifampicin and isoniazid is now recommended for all patients with new onset, uncomplicated pulmonary or extra-pulmonary TB. Ethambutol or streptomycin can be omitted in patients in whom isoniazid resistance is unlikely. Longer treatments (9-12 months) are considered for patients with meningeal disease, HIV co-infection or drug intolerance. With adherence to drug therapy and where the strain is fully sensitive, relapse would be rare.

Four drugs must be used on patients with a history of past treatment. MDR-TB treatment is complex and depends on the sensitivity of the isolate.

The patient is admitted to a negative-pressure isolation room until non-infectious and five or more drugs are used for treatment. Most patients can be treated at home. Patients can be assumed to be non-infectious after 2 weeks of quadruple therapy and where drug resistance is not expected. DOTS are recommended for non-compliant patients, MDR patients and in patients with language difficulties. DOTS therapy is recommended globally by the WHO for all patients with TB (Davidsons, 2002). MDR strains make TB more costly and difficult to treat. There is therefore a need for newer and more effective drugs that can achieve multiple goals in improving TB control (Tovaru *et al*. 2008).

Short-course therapy using 4 drugs is curative in the absence of major complications. Patients can die from infections due to miliary disease or bronchopneumonia. Mortality is increased in HIV-associated TB as a result of superimposed bacterial infection. (Davidsons, 2002).

2.13 ORAL HEALTH CONSIDERATIONS

The risk of TB transmission from patients to oral health care workers is considered to be minimal (Cleveland *et al*. 1995). However, *M. tuberculosis* is uniquely hazardous to oral health care workers because of its airborne route of transmission, lack of effective vaccination, the long and tedious treatment regimen, presence of resistant strains and the long-term sequelae of the infection. Historically, tuberculosis has been regarded as an occupational hazard for oral health care workers; presently persons who work with high-risk patients or in high prevalence communities are still considered at risk for new infection.

Standard precautions provide the fabric for strategies to prevent or reduce the risk of exposure to blood borne pathogens and other potentially infectious material. However, standard precautions are inadequate to prevent the spread of organisms through droplet nuclei 1-5 microns in diameter and additional measures are necessary to prevent the spread of *M. tuberculosis*.

The magnitude of risk varies by setting, occupational group, and prevalence of TB in the community, patient population served in the setting, procedures performed and effectiveness of TB infection-control measures. Every setting in which services are provided to persons who have suspected or confirmed TB disease should have a TB infection-control plan. The probability of a person exposed to *M. tuberculosis* becoming infected depends on the concentration of infectious droplet nuclei in the air and the duration of exposure to a person with infectious TB disease (CDC, 2005). Environmental factors such as exposure in confined spaces, inadequate ventilation and recirculation of air containing infectious droplet nuclei further increase the likelihood of transmission (American Thoracic Society, CDC, 2000). Cases with positive smears are highly infectious. Prior to the AIDS epidemic it was accepted that pulmonary cavity formation was necessary for contagiousness. However, patients with AIDS and pulmonary TB may be highly contagious in the absence of cavitations and normal chest radiographs. This results in delayed diagnosis and a greater risk of nosocomial transmission.

There is a paucity of data linking dental instrumentation to the generation of droplet nuclei containing *M. tuberculosis* (Duell and Madden, 1970; Belting *et al*. 1964). Similarly, the reported incidence of tuberculin skin test conversion among oral health care workers is low (Porteous and Brown, 1999; Mikitka *et al*. 1995; CDC, 1993). It can however be anticipated that oral health care workers and patients with infectious TB disease will generate droplet nuclei by coughing, sneezing, laughing and talking; therapeutic intervention could stimulate coughing and promote the generation of infectious particles. Since patients and oral health care workers share the same air space, the potential for the transmission of *M. tuberculosis* cannot be discounted (Naidoo and Mohammed, 2002). Infection control procedures at dental practices should include knowledge of the signs and symptoms of active TB, an updated medical history related to respiratory illness and referral of suspicious patients for medical evaluation.

Hand-washing must be done prior to and following patient contact, instruments must be sterilised and contaminated working surfaces must be disinfected with phenol and glutaraldehyde. Well-constructed, soft, pleated, high-filtration face masks must be

worn when aerosols are produced during dental treatment. Masks must be kept dry to avoid microbes passing through.

Aerosols can be reduced by avoiding the use of water spray from the triplex syringe, use of rubber dams and high volume suctions. The probable transmission of MDR TB disease from patients to two oral health care workers has been documented in the United States, and there is evidence of TB disease transmission from an oral surgeon to 15 patients following extractions (Cleveland *et al.* 1995; Smith *et al*. 1982).

The 2005 CDC guidelines for preventing the transmission of *M. tuberculosis* in healthcare facilities explicitly identify oral healthcare settings as outpatient settings in which patients with suspected or confirmed infectious TB disease are expected to be encountered (CDC, 2005). This inclusion is based on the assumption that patients with infectious TB disease may present in the dental setting for urgent or routine dental care and oral health care workers might share air space with persons with infectious TB disease or might come in contact with clinical specimens that contain *M. tuberculosis.*

Therefore, every oral healthcare facility should have a TB infection-control plan that is part of its written infection control/exposure control protocol. The TB infection-control component of an overall infection control/exposure control programme should be appropriate for the level of risk in the specific health care setting and should be based on a three-level hierarchy of administrative, environmental and respiratory-protection controls (CDC, 2005; Kohn *et al*. 2004; CDC, 2003; Cleveland *et al*. 1994).

The first and most important level in the TB infection-control program is the implementation of administrative controls which includes: (i) conducting a TB risk assessment for the oral health care setting, (ii) developing, implementing, and enforcing a written TB infection-control plan to ensure prompt detection, airborne infection isolation and treatment of persons with suspected or confirmed TB disease, (iii) implementing an ongoing training and education programme, and (iv) screening and evaluating oral health care workers who are at risk for TB disease or who might be exposed to *M. tuberculosis.*

These administrative controls are intended to reduce the risk of exposure to persons, who might have infectious TB disease, and they are essential prerequisites for the effectiveness of environmental controls and respiratory-protection controls in all settings where patients with suspected or confirmed TB disease are expected to be encountered (CDC, 2005).

Although the overall risk of oral health care workers for exposure to a patient is probably low, every oral healthcare setting should conduct initial and ongoing (annual) evaluations of TB risk for the setting and determine the demographics of the patient population served in that setting (CDC, 2005). This will determine the types of administrative, environmental, and respiratory-protection controls that are needed for the particular setting. Consultation with the local or state health department must be done.

Contact with patients with undiagnosed or unsuspected infectious TB disease is the primary risk of exposure to *M. tuberculosis* in the oral healthcare setting. A high index of suspicion and rapid implementation of precautions are essential to prevent and interrupt the transmission of *M. tuberculosis.* Specific precautions will vary depending on the setting, i.e. prevalence of TB in the community, patient population served and the type of services provided in a particular setting. The minimum requirements in a community-based oral healthcare setting is the implementation and enforcement of a TB infection-control protocol that provides (i) prompt identification of patients with suspected or confirmed infectious TB disease, (ii) separation of patients with suspected and confirmed TB disease from other oral health care workers and patients, and (iii) referral of patients with suspected and confirmed TB disease for a medical evaluation and/or required oral healthcare procedures to a facility with appropriate environmental controls and respiratory protection controls (CDC, 2005).

An essential part of administrative controls in a TB infection-control programme is the education and training of oral health care workers which include all paid and unpaid persons working in the oral healthcare setting who have the potential for exposure to *M. tuberculosis* through air space shared with persons with suspected or confirmed infectious TB disease (CDC, 2005). Risk classification for the setting will determine the need for and frequency of TB screening for oral health care workers. Oral healthcare facilities are considered medium risk settings.

All oral health care workers should receive baseline TB screening at the time of hire. Follow-up TB screening should be performed annually. Oral health care workers with positive results should be evaluated promptly for TB disease. Radiographs are also important as part of the evaluation. Preventive therapy should be offered to all personnel with baseline-positive results. Personnel with TB disease should be excluded from the workplace until they are receiving adequate therapy, their cough has resolved and their sputum smears are negative (CDC, 2005).

The concept of universal precautions is the key element of infection control in dentistry since medical history and examination cannot reliably identify all patients or carriers of infections. All patients must therefore be regarded as potentially infectious. Deferral of non-emergency care may be indicated when patients present for dental treatment with diseases such as TB and they should then be treated when they are non-contagious.

Patients requiring urgent dental treatment should be referred to a facility with TB engineering controls and a respiratory protection programme. Patients should wear a surgical mask or be instructed to cover mouth and nose when coughing or sneezing when they are not being evaluated. In order to minimise the spread of respiratory or other diseases in dentistry emphasis should be placed on vaccination, use of particulate respirators and adequate ventilation. The BCG vaccine is an effective measure that can help control the spread of TB and should be administered to oral health care workers in geographic regions or clinical settings where there is a high prevalence of TB.

In addition the surgery should have good ventilation; aerosols should be controlled by high volume externally vented aspirators and wearing of particulate respirators. Facemasks routinely used by oral health care workers may not always provide an effective means of preventing infection. Oral health care workers need to be alert to signs and symptoms of TB and refer such individuals for appropriate medical health care (World Dental Federation (FDI), 2003). A TB screening programme should be established for the protection of both workers and patients. The prevalence of TB in the community or patient population indicates a potential risk for occupational exposure to TB.

Tuberculin skin testing data should be evaluated regularly to enable the dental personnel to evaluate the effectiveness of current infection control practices (Cleveland *et al*. 1995).

The resurgence of TB as a public health problem, the explosive outbreaks of TB among AIDS patients, reports of transmission to staff and the emergence of drug resistant strains have refocused attention on the risk to oral health care workers and has rekindled interest in this disease among oral health care workers. However, much research has focused on pulmonary and extra-pulmonary TB involving the abdomen and spine and there is a paucity of literature on the head and neck region. Extra-pulmonary presentations form a significant proportion of new cases concomitant with HIV epidemic. The increase in numbers of HIV seropositive individuals and the late diagnosis of TB in these patients because of atypical signs and symptoms, suggest that oral health care workers may be unknowingly treating infected patients who pose a risk. The generation of aerosols in modern dentistry is a recognised risk for transmission of infection which is droplet spread. Systemic symptoms may be absent and oral lesions may be the first manifestation of the disease. Therefore oral health care workers need to be aware of TB in the head and neck region and its varied manifestations.

CHAPTER 3: AIMS AND OBJECTIVES

3.1 AIM

To determine the extent to which tuberculosis presents in the head and neck region.

3.2 OBJECTIVES

- To retrospectively ascertain the presentation of head and neck tuberculosis.
- To describe the management and outcomes of head and neck tuberculosis.

CHAPTER 4: METHODOLOGY

This chapter presents the aims and objectives of the study, the study design, sampling, matching and inclusion criteria. In addition, the survey method, development and piloting of the data capture sheet, data entry and method of analysis are described.

4.1 INTRODUCTION

The resurgence of TB as a public health problem, especially in South Africa, has rekindled interest in this disease among oral health care workers. The TB epidemic in South Africa is likely to be exacerbated over the next few years due to the high prevalence of HIV/AIDS. Much research has focused on pulmonary and extra-pulmonary TB involving the abdomen and spine and there is a paucity of literature on the head and neck region. Extra-pulmonary presentations form a major proportion of new cases concomitant with the HIV epidemic. Systemic symptoms may be absent and oral lesions may be the first manifestation of the disease. Therefore oral health care workers need to be aware of TB in the head and neck region and its varied manifestations.

This study was attempted due to the fact that there is no epidemiological data available on head and neck TB in South Africa. With this background, and the paucity of literature related to dentistry, the aim of this study was to determine the extent to which tuberculosis presented in the head and neck region in Kwa-Zulu Natal.

4.2 LIMITATIONS OF STUDY

The study could not be conducted as a prevalence study as originally planned, but instead reports on the descriptive data of a convenience sample of 104 patients presenting with head and neck tuberculosis.

The initial plan for data collection was to be over a period of 10 years and information was to be obtained from the various hospitals in the Durban area. The hospitals approached were King Edward, Addington, Albert Luthuli, King George, RK Khan and Prince Mysheni Unfortunately this was not possible. King Edward, RK Khan and

Prince Mysheni refused permission saying that they did not see patients with head and neck TB although they had an Ear, nose and throat (ENT) Department. Addington refused permission on the grounds that there were too many researchers at their hospital. The reason given by Albert Luthuli was that all their records were on computer and that they could not give access to their passwords in order to access records. Permission to access data was only granted by King George Hospital. It was not an easy task to identify patients with head and neck TB from the patient register and this would have entailed going through many thousands of records to find cases and this would have been like "looking for a needle in the haystack". An attempt was then made to identify patients with positive head and neck TB through a provincial lab search at Albert Luthuli Hospital. This too proved futile as the researcher was not allowed to access the data herself and the searches were done by staff. They could not identify any patients from their system with positive head and neck TB.

Due to the difficulty experienced in obtaining data from hospital records it was then decided to source patients from private practices. Contact was made with Physicians, Surgeons and the ENT society through their chairperson. The study protocol and ethical approval was presented to them and they were then prepared to assist with the research. Due to the enormity of the task and subsequent advice from one of the ENT specialists, contact was then made with Lancet Laboratory to assist in identifying patients with positive TB in the head and neck region. Records from January 2008 to present could only be accessed. Hence, the present study reports on cases diagnosed over a period of fourteen months. Once the patients were identified, the various practices were contacted for permission to access patient records.

4.3 STUDY DESIGN

This present study was a descriptive, retrospective, record based study on a cohort of TB patients that presented with head and neck TB. Information from patient records was extracted and recorded in a structured data capture sheet (Appendix 1). Data from patients attending the private ENT specialists, physicians and surgeons was recorded.

It was anticipated that the descriptive study would summarise routine data and would quantify the extent of a health problem or the burden of disease in a population. This descriptive study was limited to the prevalence of the occurrence of disease in a population. Descriptive studies provide information to health care planners that will help them develop appropriate services, allocate resources, decide on priorities, and target certain populations. A retrospective study would shorten the time needed to conduct a cohort study as it makes use of historically or previously compiled data.

4.4 STUDY SITES

Private practices of four ENT specialists, eight Physicians and seven Surgeons.

4.5 SELECTION OF STUDY POPULATION

The study population was a convenience sample including all patients attending the various practices. The study sample included all patients diagnosed with head and neck TB at these practices.

4.6 STUDY POPULATION AND SAMPLING

A search was conducted at the lab on 36 practices in the Durban region in order to identify the patients with TB of the head and neck region. Of these searches only 26 of the practices had patients with positive head and neck TB. Of these 26 practices only 19 of them allowed me access to patient records. The study sample included all patients diagnosed with head and neck TB at these practices.

4.7 INCLUSION CRITERIA

Patients diagnosed with TB and with head and neck TB.

4.8 INSTRUMENT

A structured data capture sheet was the method chosen for collecting the data (Appendix 1). The data capture sheet was designed to ensure that it suited the aims and objectives of the study, was clear, simple and unambiguous, minimized potential errors from the researcher and coder and enabled efficient, meaningful analysis of the acquired data.

The structured data capture sheet was used to determine the:-

- Age and gender of the patient
- Presenting symptoms
- Type of examination and investigations done
- Type of head and neck TB
- Treatment and management of head and neck lesions
- Other sites (apart from head and neck) presenting with TB
- Response to treatment

4.8.1 Development of the data capture sheet

Planning of the data capture sheet began in February 2008. It was developed from information obtained from the review of literature on head and neck TB. For the purpose of this study, the data gathered was divided into six sections: (i) demographic – age and gender of the patient; (ii) HIV/AIDS status; (iii) presenting signs and symptoms; (iv) examinations and investigations; (v) head and neck sites and other sites involved; (vi) treatment provided and (vii) the outcomes.

4.8.2 Piloting the data capture sheet

A pilot study was conducted to test the data capture sheet in terms of practicability and relevance. The pilot study was carried out to:

(i) test the suitability of the method of collecting the data
(ii) test how long it would take to record information from patient cards
(iii) check the adequacy of the data capture sheet
(iv) check that all the parameter measurements were clear and unambiguous
(v) ensure that no major item had been omitted and
(vi) remove any items that did not yield usable data.

4.8.3 Preparation of the final draft

After the pilot study, irrelevant and problematic items was identified and deleted or reformulated. A final draft of the data capture sheet was then printed and used for the final study.

4.9 DATA COLLECTION METHODS

Once the patients with positive TB in the head and neck region were identified at the lab, their cards were obtained from the various practices and the information was recorded in the data capture sheets. The following information was recorded on the data capture sheets: patient number, age, gender, HIV/AIDS status, presenting signs and symptoms, types of examinations and investigations, head and neck sites and other sites involved, treatment provided and the outcomes.

4.10 VALIDITY AND RELIABILITY

The researcher was the only investigator involved in the gathering and interpretation of the data thereby assuring the standardized recording of all the information presented. To ensure validation of the data capture sheets, the instrument was subjected to a test-retest procedure (by repeatedly administering the scales to the same sample within a short period).

4.11 DATA ANALYSIS

Following the literature review, the study selected the relevant statistical tests required and the data was processed after the information was loaded onto the SPSS15 system and analysed by the researcher. Interpretation of all the statistical data was done by the researcher with assistance from a statistician.

4.12 PROCEDURES

4.12.1 Establishing contacts

Access to the participating hospitals was initially made by a telephone call followed by a visit to meet the staff working at the ENT clinics at these hospitals. A letter (Appendix 2) with the ethical approval and protocol was then sent to hospital managers. A letter of approval was required from the various hospitals that had to be sent to Health Research Ethics Committee at the Department of Health for final approval to access data at these hospitals. Permission was granted by only one of the six hospitals identified for this research project. The letters (Appendix 2, Appendix 3 and Appendix 4) with the protocol was then sent to Health Research Ethics Committee at the Department of Health. A final approval letter (Appendix 5) was received from Health Research. This letter was then forwarded to the hospital that had granted permission to access records. An introduction of the researcher, the basic aims and objectives of the study, what participating in the study would involve and how long the examination would take, were explained. It was emphasized that strict confidentiality would be maintained at all times and that the results of the study would be presented in a manner that ensured anonymity.

Once signed, approval had been obtained from the Hospital managers and arrangements were made to access patient clinical records at a time convenient to the participating hospital.

When obtaining data from the hospital proved futile, contact was then established with the private ENTs, Physicians and Surgeons to access data at their private practices. The data capture sheet (Appendix 1) together with the letters (Appendix 2 and 3) were sent to the private practitioners. When identifying patient records with positive head and neck TB proved difficult at the private practices, contact with Lancet Laboratory was established to identify these patients.

4.12.2 Ethical considerations

The study protocol was submitted to the Senate Research Ethics Committee of the University of the Western Cape for ethical approval. Approval was granted through a letter (Appendix 3). Permission was sought from the relevant persons to access records. It was emphasized that strict confidentiality would be maintained at all times.

4.13 CONCLUSION

This chapter described the selection of the study population which included a laboratory search to identify the patients. Establishing contacts and accessing information was not an easy task - practitioners were very uncooperative and refused permission. The instrument developed to collect the data was a focused, structured data capture sheet in six parts and the piloting of it is described in this chapter.

CHAPTER 5: RESULTS

This chapter presents the findings of the study. It describes the demography of the sample of patients that presented with head and neck TB, the association with HIV, the presenting complaints, examinations and investigations that were performed, the head and neck sites that were involved, the treatment that was carried out and the outcomes of patient management.

5.1 DEMOGRAPHY

The study included one hundred and four cases of TB of the head and neck region from nineteen private practices in the Durban region. The regions included the city centre, north, north central, south and south central. The twelve practices in the city centre and surrounding area made up the majority of the patients (69%), four practices in the south central region made up 4% of the patients, the north central region where five practices were visited made up 24% of the patients and the north region where one practice was visited made up 3% of the patients. Forty one patients (39.4%) were male and sixty three (60.6%) were female. The age ranged from one year to sixty one years. TB of the head and neck region presented most commonly in the thirty-one to forty year age group (Table 6), which comprised of 43% of the total number of patient records examined.

Table 6: Age Distribution of TB Head and Neck

Age Range	Percentage of Patients
0 – 20	7%
21 – 30	23%
31 – 40	43%
41 – 50	20%
50 and above	7%
Total	100%

Seventy seven (74%) of the patients with head and neck TB were of African (Black origin) and twenty seven (26%) were of Asian origin. Patient records indicated a greater preponderance to females presenting with head and neck TB (sixty two (42%) of females in comparison to forty two (32%) males). Thirty five (33.7%), which made up a third of the patients, was confirmed with HIV. Lymph nodes which were found in ninety three (89.4%) of the patients was the most common site of head and neck TB.

5.2 PRESENTING COMPLAINTS

Thirteen patients (12.5%) presented with fever, two (1.9%) with weight loss, seventeen (16.3%) with cough, five (4.8%) with hoarseness, two (1.9%) with odynophagia, ten (9.6%) with dysphagia, and eight (7.7%) with otalgia. The presenting complaints of forty seven (45%) of the patients were not recorded. Other signs and symptoms included a neck abscess, neck mass, headaches and pain. The details of the presenting complaints at the individual sites are described below.

5.3 EXAMINATIONS AND INVESTIGATIONS

Investigations included one (1%) needle aspiration, thirty five (33.7%) chest x-rays, fifteen (14.4%) sputum culture, five (4.8%) PPD, twelve (11.5%) pus culture and sensitivity. One hundred and two (98.1%) excision biopsies and one hundred and three (99%) histological examinations were done. Other investigations included full blood surveys, scans, ultrasounds, bronchoscopy and laryngoscopy.

5.4 HEAD AND NECK SITES OF TUBERCULOSIS

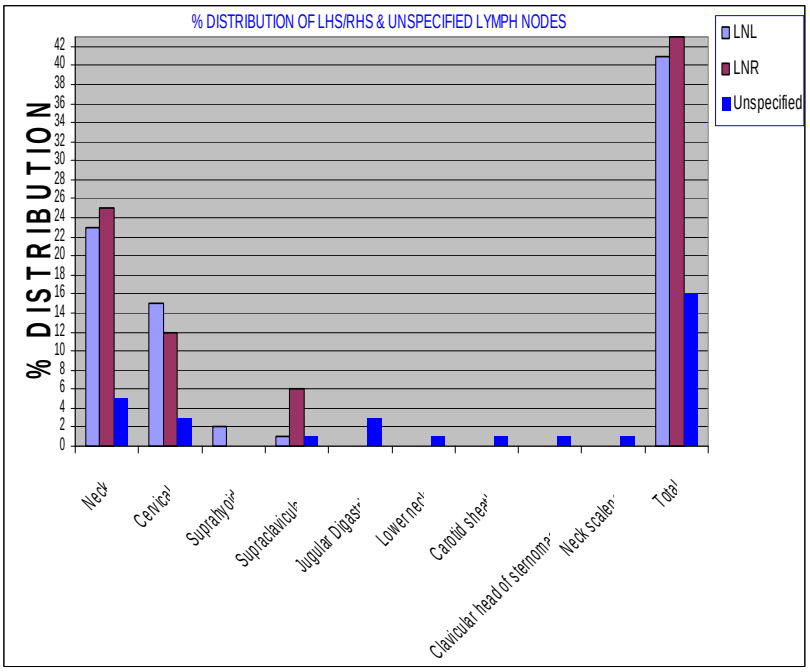
TB of the head and neck presented most commonly in the lymph nodes of the head and neck region (Table 7). The second most common site was the tonsil. Other sites included the ethmoid sinus and the mastoid process. No patients were identified with TB of the cervical spine, tongue, hard palate, soft palate, mandible, tempero-mandibular joint, maxilla, buccal mucosa, gingiva, floor of the mouth and lips.

Table 7: Percentage distribution of the head and neck sites

Head and neck site	Number	Percentage
Head and neck lymph nodes	93	89.4%
Tonsil	5	4.8%
Larynx	2	1.9%
Ear	2	1.9%
Parotid Gland	1	1%
Nose	1	1%
Total	**104**	**100%**

The presentation of lymph nodes was slightly higher (Figure 1) on the right side of the head and neck region, twenty three (25%), as compared to twenty one (23%) on the left hand side. The specific side of sixteen (16%) of the lymph nodes were not recorded (Figure 1). This is reflected as unspecified side (16%).

Figure 1: Percentage distribution of lymph nodes on the left and right side of neck and unspecified side



5.5 OTHER SITES

Additional sites of TB that were found were twelve (11.5%) with TB of the lung, five (4.8%) with TB of the abdomen and one (1%) in the liver.

5.6 TREATMENT

Just over two thirds (62.5%) of the patients treatment for chemotherapy, isoniazid, rifampicin, pyrazinamide, ethambutol, ARTs and radiotherapy was not recorded. Of the patients that were recorded one, (1%) had chemotherapy, eleven (10.6%) were put on Isoniazid therapy, twenty nine (27.9%) were on Rifampicin, thirty one (29.8%) on Pyrazinamide, ten (9.6%) on Ethambutol, seventeen (16.3%) were on ARTs and one hundred and three (99%) had surgery performed.

5.7 OUTCOMES

Of the sample of 104 patients, five (4.8%) had survived and were in remission, four (3.8%) were lost to follow up, eighty (76.9%) were transferred to their referring doctors, three (2.9%) were not evaluated and 12 (11.5%) were still on treatment.

5.8 COEXISTING DISEASE

Just over ten per cent (11.5%) had co-existing pulmonary TB, five (4.8%) had TB of the abdomen and 1 (1%) had TB of the liver. A third (33.7%) was HIV positive – the majority of the HIV positive patients (97%) presented with TB of the lymph nodes. In addition to TB of the head and neck, nearly a third (29%) of the HIV positive patients had associated lung TB, three (9%) had associated TB of the abdomen and one (3%) had TB of the liver.

5.9 RESULTS FOR INDIVIDUAL SITES

5.9.1 Tuberculosis of the lymph nodes

Majority of the patients which was 93 (89.4%) suffered from tubercular lymphadenitis. Six patients (7%) presented with discrete cervical node swelling, six patients (7%) presented with matting and four patients (5%) with ulceration and discharge. The most commonly involved lymph node group was the cervical left (15% - Figure 1). One of the patients that presented with a neck abscess was a one year female child who was confirmed with HIV. Tests included sputum, excision biopsy and histology.

5.9.2 Tuberculosis of the larynx

The two patients with TB of the larynx consisted of a sixteen year old female and a thirty two year old male patient. The presenting signs and symptoms were cough, hoarseness, dysphagia and discomfort in the throat. Investigations for these patients included sputum tests, PPD, excision biopsy and histology.

5.9.3 Tuberculosis of the tonsil

These were all female patients between twenty five and thirty five years old. These patients presented with discomfort, sore throat, dysphagia, hoarseness, otalgia and cough. One patient presented with associated lymph node. Investigations included excision biopsy and histology.

5.9.4 Tuberculosis otitis media

The two patients that presented with TB in this region were a forty five year old male and a fifty year old female patient. Both patients presented with otalgia, one suffered from hearing impairment and deafness and the other had a discharge from the ear. The female patient also had TB of the left mastoid and had to have a mastoidectomy performed. Chest x-rays, pus culture, excision biopsy and histology were included in the investigations.

5.9.5 Tuberculosis of the Parotid

This was found in a fifty year old male patient. The patient presented with a lump in the neck region and had an excision biopsy and histopathological examination done to confirm TB.

5.9.6 Tuberculosis of the nose

The presenting signs and symptoms for this forty two year old male patient were headaches and pain in the nasal passage. Investigations included an excision biopsy and histopathological examinations. Two patients, a forty one year old female and a sixty one year old male presented with TB in the ethmoid sinus. Presenting signs and symptoms included otalgia, hoarseness, odynophagia, dysphagia, nose block, bleeding, sneezing, headaches and phlegm. Chest x-rays, excision biopsy, and histopathological examination were the investigations that were performed.

5.10 CONCLUSION

The analysis of the results was described in this chapter. A major proportion of the information such as presenting signs and symptoms and treatment administered was not recorded on the cards. This was especially common in the data obtained from the surgeons. These patients were transferred back to their referring doctors for further management.

CHAPTER 6: DISCUSSION

This chapter discusses the findings of the present study. The study was not a prevalence study as originally planned, but rather a descriptive study - one of a sample of patients with head and neck TB from private practices in the Durban area over a fourteen month period.

The causes for the resurgence of TB worldwide vary from one country to another and include: co-existing HIV infection, multidrug resistance, failure to comply with treatment, social disruption due to war and economic migration and economic poverty (Menon *et al*. 2007). About two thirds of the population in South Africa are infected with TB. South Africa was ranked fifth among the world's twenty two high-burden TB countries by the WHO. The national incidence rate was an alarming 718/100 000 in 1998 (Erstad, 2006).

Three risk factors were identified for extra-pulmonary TB: being female, being African (Black) and being HIV positive. The observation made that females are an independent risk factor for having extra-pulmonary TB is contrary to the traditional understanding that females are more resistant to TB than males. The observation was based mainly on animal studies and the reported global sex-difference in TB case rates (i.e. in general, a higher proportion of TB case notifications worldwide are for male than for female patients). The lower notification rate for females does not necessarily mean that females are more resistant to TB than the males, but may be the result of under diagnosis or underreporting of TB in females as a result of various social and or cultural factors, including the stigmatization of females with TB and their consequent impaired access to health care. This situation is often seen in developing countries (Yang *et al.* 2004). Few studies in the past have specifically focused on a comparison of extra-pulmonary TB among males with extra-pulmonary TB among females. The fact that a biased distribution of any particular type of extra-pulmonary TB that affects only women was not observed, the biological credibility of the finding that being female is strongly associated with extra-pulmonary TB remains to be determined through further investigations.

There have been reports of an association between non-Hispanic black race and extra-pulmonary TB in earlier studies of HIV infected subjects (Yang *et al*. 2004). The applicability of these results to other populations is uncertain. This association needs confirmation.

The present study included both HIV positive and HIV negative patients with extra-pulmonary TB. HIV infected patients are more vulnerable to transmission of mycobacterium from others with active TB, and those with latent disease have a high risk of reactivation. The incidence of TB is about a hundred times more in HIV infected patients than that of the general population. Therefore the diagnosis of TB lymphadenopathy must be seriously considered in all HIV infected patients who present with an enlarging neck mass (Lee and Schecter, 1995).

In the present study, extra-pulmonary TB was found to be more common in the thirty-one to forty-year-age group and this is similar to that reported by Yang *et al*. (2004) whose study consisted of a total of 705 patients diagnosed with tuberculosis.

Cervical lymph nodes have been reported to be the most common site in the head and neck region to be affected by TB (Prasad *et al*. 2007; Nohrstrom *et al*. 2007; Munck and Mandpe, 2003). This finding is supported by the present study. The most commonly involved cervical lymph nodes could not be identified as the specific sites were not recorded on all the patient records but more generalised terminology was used. In this study, the clinical presentations of the lymph nodes included discreet cervical lymph node swelling, matting, ulcerations and discharge. TB of the head and neck lymph nodes was slightly higher on the right side.

The second most common presentation was the tonsils. There is a paucity of literature on TB of the tonsils due to the fact that it is exceedingly rare. Reasons for this include the fact that tonsillar TB was common at the beginning of the century and was related to *M. bovis* infections acquired by drinking infected milk – with the advent of the pasteurization of milk this entity is now extremely rare (Munck and Mandpe, 2003). TB of the tonsils was fairly common in the pre-antibiotic era (Waldman, 1982).

Prior to the antibiotic era, laryngeal TB was considered to be the most common disease of the larynx that was seen in more than a third of patients with pulmonary TB. The disease is fairly rare today and occurs in less than 1% of tuberculosis cases (Munck and Mandpe, 2003). Patients present with hoarseness, dysphagia, cough and discomfort in the throat. Laryngeal TB should be considered in any patient with unexplained hoarseness, weakened voice, and pain with swallowing which may radiate to the ear as well as odynophagia. Laryngeal TB may involve any site including the vocal cords, ventricular bands and epiglottis.

Tuberculous otitis is the next most common form of TB in the head and neck after TB of the larynx (Sierra *et al*. 2000). Aural TB is uncommon and difficult to diagnose because the disease presents like other chronic suppurative otitis media. Typical features include painless otorrhoea; central perforation; pale, abundant middle ear granulations; severe conductive or profound hearing loss; and facial palsy. Bone necrosis and sequestration in the mastoid are also common findings. With super-imposed infection there may be otalgia, foul smelling infection and acute mastoid infection and fistulisation. (Prasad *et al*. 2007). In this study eight patients presented with otalgia, two with hearing impairment and two with discharge from the ear. Infection of the mastoid process was reported in one patient.

Tuberculosis of the oral cavity was not reported in the sample of the present study.

The definitive diagnosis for the majority of the patients was established by histological examination. Tissues should be sent for histological examination to make a final diagnosis, if the index of suspicion is high and all other tests for TB are negative.

More than two thirds of the patients in this study were transferred for further treatment to their referring doctors and therefore the treatment provided for TB was not recorded. Treatments that were recorded included Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. This is in keeping with the recommended treatment regime. Patients that were HIV positive were referred for highly active antiretroviral therapy (HAART). There were no follow-ups recorded for these patients; therefore the outcomes from the treatment could not be established.

CHAPTER 7: CONCLUDING REMARKS

Tuberculosis is a challenging disease and is on the increase. TB of the head and neck remains an important diagnosis. It may not be as rare as once thought and is the commonest site of extra-pulmonary TB. The diagnosis is often misdiagnosed. A high index of suspicion of TB is important in the differential diagnosis of slow-to-heal wounds, undiagnosed neck lumps, hoarseness and otorrhoea and especially in HIV positive patients with any enlarging neck mass. A biopsy is usually necessary for diagnosis. Successful outcome depends upon appropriate chemotherapy and timely surgical intervention when necessary. It is in the best interest of the oral health care worker to be fully cognizant of all the various presentations of head and neck TB.

A high index of suspicion can help direct investigations, allowing early diagnosis and quick commencement of appropriate treatment. TB positive patients should be treated in consultation with a physician. Oral health care workers must understand the medical management of TB. With the rising incidence of TB, especially in South Africa, it is likely that they will be confronted with patients at risk for TB and those patients who have been or who are already on anti-tuberculosis therapy.

The cornerstone for the effective control of TB is the effective treatment of persons who have active TB. Oral health care facilities have the opportunity for TB screening, which as yet, has not been tapped in to its fullest extent in a developing country setting like South Africa where TB is endemic. Oral health care workers can play a role in this control by identifying patients who may need TB treatment or prophylaxis and referring those patients for medical evaluation. TB infection control policies should be developed for each dental setting based on risk assessment. This should include a review of the community TB profile, which can be obtained from the Department of Health, and the number of the TB patients treated in the facility.

Five risk categories are defined: minimal, very low, low, intermediate and high risk. High risk settings are those in which there has been evidence of transmission of TB (Cleveland *et al*. 1995).

Following risk assessment, policies developed should include provisions for detecting and referral of patients with active TB who require urgent dental care. They should also include provision for education, counselling and screening of oral health care workers. Routine assessment of all dental patients should include whether patients have a history of TB and signs and symptoms suggestive of TB.

For oral health care facilities that provide care to populations at high risk for TB, controls to decrease the risk of transmission should be considered: ventilation and air flow considerations, such as high-efficiency particulate air filters or ultraviolet germicidal irradiation (CDC, 1998). Use of disposable tubes and masks for nitrous oxide sedation to prevent patient-to-patient transmission, TB positive patients should be scheduled for morning or late in the afternoon appointments to reduce the possibility of patient-to-patient transfer in the waiting areas.

While the risk of TB transmission in the oral health setting is probably low, the consequences of exposure can be substantial. Oral health care workers have a duty to take appropriate precautions to protect themselves, their staff and their patients from the risk of cross infection. The implementation of infection control policies is critical to the provision of such protection.

Oral health care workers must be knowledgeable about the potential risks of occupation exposure, the importance of practicing universal infection control and post-exposure management strategies for those potentially exposed to TB. A clear, written TB infection control protocol should promote the importance of surveillance in the oral health setting. Referral and integration of TB screening in high HIV and TB prevalence areas will provide early diagnosis, treatment of TB and possibly prevention and reduced risk of nosocomial infection.

At present there are no specific guidelines for infection control for South Africa. Guidelines need to be actively promoted and established. These guidelines need to be pertinent to South Africa and must be flexible enough to fit individual circumstances. Recommendations should be based on available resources and be sensitive to the powerful social, political and psychological forces behind the public and professional response to the TB pandemic.

As noted in the introduction to this thesis, HIV increases the susceptibility of the HIV positive person to TB. Educating communities and patients to recognise symptoms of TB and to seek health care and further investigations should be routine in all settings providing care for patients, especially HIV-infected persons. Coordination and communication between HIV and AIDS and TB programmes must be prioritised.

There is much information on TB in South Africa and there should not have been the limitations to the gathering of the study data. The problems experienced could have been avoided if patient data was properly recorded and easily accessible to researchers. It is recommended that information systems be improved for easy identification of specific conditions, doctors should keep proper, legible and comprehensive notes for their patients and that all data should be accessible to bona-fide researchers particularly in the public sector hospitals.

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APPENDIX 1: DATA CAPTURE SHEET

1. Patient no.

2. Age:

3. Gender: Male Female

4. HIV/AIDS (confirmed): Yes No

Presenting signs and symptoms

Condition		**Yes**	**No**	**Not recorded**
5	Fever			
6	Weight loss			
7	Cough			
8	Hoarseness			
9	Odynophagia			
10	Dysphagia			
11	Otalgia			
12	Other:			

Type of examinations and investigations

Investigations		**Yes**	**No**	**Not Recorded**
13	Needle aspiration cytology			
14	Chest x-ray			
15	Sputum culture			
16	Purified protein derivative (PPD)			
17	Pus – culture & sensitivity			
18	Excision biopsy			
19	Histopathological examination			
20	Other:			

Head and Neck sites of tuberculosis

Location		Yes	No	Not recorded
21	Lymph nodes Specify:			
22	Tonsil			
23	Larynx			
24	Cervical spine			
25	Parotid glands			
26	Tongue			
27	Hard palate			
28	Soft palate			
29	Mandible			
30	TMJ			
31	Maxilla			
32	Nose			
33	Tubercular otitis media			
34	Buccal mucosa			
35	Gingiva			
36	Floor of mouth			
37	Lips			
	Other:			

Other sites

Location		Yes	No	Not recorded
38	Lung			
39	Brain			
40	Spine			
41	Abdomen			
42	Skeletal			
43	Liver			
	Other:			

Treatment provided

Treatment		Yes	No	Not recorded
44	Chemotherapy			
45	Isoniazid			
46	Rifampicin			
47	Pyrazinamide			
48	Ethambutol			
49	ART			
50	Surgery			
51	Radiotherapy			
	Other:			

Outcomes

Outcome		Yes	No	Not recorded
52	Survived in remission			
53	Recurrence			
54	Lost to follow up			
55	Died			
56	Defaulted			
57	Treatment Failed			
58	Transferred			
59	Cured			
60	Not evaluated			
	Other:			

APPENDIX 2: CONSENT TO ACCESS RECORDS AND TO CARRY OUT RESEARCH STUDY

INFORMATION SHEET

TO WHOM IT MAY CONCERN

I, Ms M Reddy, am a Dental Therapist working at the Oral and Dental Training Centre. At present I am studying part time and am currently a Masters student at the Department of Community Dentistry, University of Western Cape.

The resurgence of TB as a public health problem has rekindled interest in this disease among oral health workers (OHW). However, much research has focused on pulmonary and extra-pulmonary TB involving the abdomen and spine and there is a paucity of literature on the head and neck region. Extra-pulmonary presentations form a major proportion of new cases concomitant with HIV epidemic. Systemic symptoms may be absent and oral lesions may be the first manifestation of the disease. Therefore oral health workers need to be aware of TB in the head and neck region and it's varied manifestations.

For my research project, I have undertaken to do a retrospective record-based study on the prevalence of head and neck tuberculosis in Durban over a twelve year period to determine the presentation of head and neck tuberculosis and describe it's management. This study has not been carried out in Durban before. It is important and will be of great value to the medical and dental profession regarding early diagnosis and management.

In order to be able to carry out this study I will need access to patient records. All information gathered in the study will be treated as strictly confidential. No one will have access to this information except me, the principal investigator. No names will be used in the reports of this study. All information collected will be maintained and stored in such a way as to keep it as confidential as possible.

If you have any questions or queries regarding the proposed study please do not hesitate to contact me, Ms M Reddy on Tel: 031-2426214 work, 031-2628623 home, cell: 084 584 4288.

Thanking you in advance for your co-operation.

Yours sincerely

_____

Ms M Reddy

APPENDIX 3: ETHICS APPROVAL LETTER FROM THE UNIVERSITY OF THE WESTERN CAPE

Department of Community Oral Health
Faculty of Dentistry & WHO Collaborating Centre for Oral Health

UNIVERSITY OF THE WESTERN CAPE
Private Bag X1, Tygerberg 7505
Cape Town
SOUTH AFRICA

25th June 2008

TO WHOM IT MAY CONCERN

Re: Ms M Reddy - MSc (Dent) in Dental Public Health

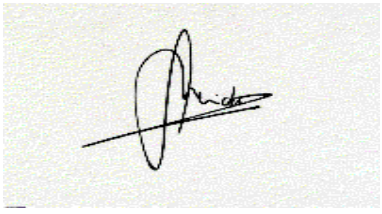
This letter serves to confirm that Ms M Reddy is a post-graduate student on above-mentioned course at the Faculty of Dentistry, University of the Western Cape.

Her student number is **2874099**

Her research project has been passed by the Senate Research Ethics Committee of the University with the registration number **08/4/11**

Should you require any additional information, do not hesitate to contact me on tel: 27-21-937 3148 (w) 686 2720 (h); fax: 27-21-931 2287 or email: suenaidoo@uwc.ac.za.

Yours sincerely



Professor Sudeshni Naidoo
Course Co-ordinator

APPENDIX 4: APPROVAL LETTER FROM KING GEORGE V HOSPITAL

DEPARTMENT OF HEALTH
PROVINCE OF KWAZULU-NATAL

KING GEORGE V HOSPITAL

PO DORMERTON,4015

75 STANLEY COPLEY DRIVE, SYDENHAM, DURBAN

Enquiries: Dr S Maharaj	Telephone Number: (031) 2087121 Ext: 356	Fax Number: (031) 2099586
Email:shamin.mahraj@health.gov.za	Your Reference :	Date: 30 June 2008

For Attention: Ms M Reddy
Post Graduate Student
University of Western Cape

Dear Ms M Reddy

REQUEST FOR PERMISSION - ACCESS TO PATIENT INFORMATION AT KING GEORGE V HOSPITAL

1. Your letter dated 30 June 2008 refers.

2. Permission is granted for the above mentioned purpose. Please find attached copy of indemnity form for completion and submission by yourself prior to undertaking the study.

3. Your attention is once again drawn to the maintenance of confidentiality as discussed.

4. Arrangements should be made for you to work with patient files and staff in the MDR TB Department.

DR S B MAHARAJ
MEDICAL MANAGER

APPENDIX 5: APPROVAL LETTER FOR RESEARCH PROPOSAL – DEPARTMENT OF HEALTH

HEALTH
KwaZulu-Natal

Health Research & Knowledge Management sub-component
10 – 102 Natalia Building, 330 Langalibalele Street
Private Bag x9051
Pietermaritzburg
3200
Tel.: 033 – 395 2805
Fax.: 033 – 394 3782
Email.: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference: HRKM 057/07
Enquiries: Mr X. Xaba
Tel: 033-395 2805

10 September 2008

Dear Ms Reddy

Subject: Approval of a Research Proposal

1. The research proposal titled **'Tuberculosis in the head and neck in Durban, KwaZulu Natal'** was reviewed by the KwaZulu-Natal Department of Health. The proposal is hereby **approved** for research to be undertaken at King George hospital.

2. You are requested to undertake the following:
   a. Make the necessary arrangements with the hospital before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mr X. Xaba.

Yours Sincerely

Dr. S.S.S. Buthelezi
Chairperson: Provincial Health Research Committee
KwaZulu-Natal Department of Health