UNIVERSITY OF THE WITWATERSRAND

COMPARATIVE OUTCOMES BETWEEN HIV POSITIVE AND NEGATIVE ENDODONTIC PATIENTS

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DECLARATION

I hereby declare that this dissertation is my work. It is being submitted for the degree of Master of Science (dentistry) in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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Saidah Tootla

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LIST OF ABBREVIATIONS

HIV:	**Human Immuno Deficiency Virus**
AIDS:	**Acquired Immuno Deficiency Syndrome**
BPE:	**Before present era**
WHO:	**World Health Organization**
CDC:	**Centre for disease control**
ART:	**Antiretroviral Therapy**
NaOCl:	**Sodium hypochlorite**

ABSTRACT

Purpose: To compare the presenting symptoms and the outcomes of root canal therapy between HIV positive and HIV negative endodontic patients over a 6-12 month period.

Methods: Fifty-nine HIV negative and 46 HIV positive patients presented for endodontic treatment. Signs and symptoms were noted and compared for both groups of patients, together with demographic data and CD4 counts for the HIV positive patients. Endodontic procedures were evaluated after an 18-month period. Endodontic treatment was assessed using clinical factors (palpation, percussion, sensitivity to hot and cold, swellings, excessive bleeding), and radiographic factors (periapical radiolucency, root resorption, periodontal ligament space).

Results: There was no statistically significant difference in the preoperative presenting symptoms of endodontic infections/conditions between HIV positive and HIV negative patients. The prevalence of radiographic caries in the presenting teeth was only 24% in the HIV positive patients compared with 95% in the HIV negative patients. For the HIV positive patients, the treatment time required to resolution of the endodontic infection was nearly twice (113 minutes) that of the HIV negative patients (52 minutes). Amongst the HIV positive patients still experiencing symptoms at 18 months, pain was more severe in those patients with lower CD4 counts (significance at the 90% level of confidence).

Conclusion: Within the limitations of this study the following conclusions emerge:

1. Although the success rate was lower over the period of this study in HIV positive patients, the rate is sufficiently high to warrant treatment.
2. Patients who are HIV positive may present with more severe symptoms and during treatment more bleeding may be expected.
3. In keeping with best practice for immuno-compromised patients, it would be advantageous to put HIV positive patients on antibiotic cover during treatment.
4. The process of anachoresis may explain the high incidence of endodontic infections in teeth with no history of trauma or caries in the HIV positive group.

CHAPTER 1: ENDODONTICS

Endodontics is “That branch of dentistry concerned with the morphology, physiology, and pathology of the human dental pulp and peri-radicular tissues. Its study and practice encompass the basic and clinical sciences including biology of the normal pulp, the aetiology, diagnoses, prevention, and treatment of diseases and injuries of the pulp and associated periradicular tissues.” [1] The purpose of this chapter is to introduce endodontics from a historical and clinically progressive perspective.

1.1 A brief history of endodontics

It is assumed that endodontics may have been practiced as early as the second or third century BPE. A skull found in the Negev Desert in Israel had a bronze wire in one of its teeth which may have been used to treat an infected pulp. Other evidence shows that pulp chambers were drained to relieve pain and pressure in the first century of the present era. Advancements in endodontic practice were halted by controversial opinions such as those of William Hunter, a physician who in 1910 accused the dental profession of contributing to ill health by the kind of dentistry practiced at the time, naming a long list of diseases which he attributed to oral sepsis from dentistry in general.[2]

Although at that time there were apparently some scientific grounds for his assertions some members of the medical profession used Hunter’s opinion as a means of shifting responsibility to the dental profession for those diseases and illnesses for which there was no available cure. It was easier to order the removal of teeth in the hope that the

patient would benefit than to determine the cause and develop a remedy. The result was the wholesale extraction of teeth. In fact, some urged not only simple extraction but surgical removal. [2] Today it is widely agreed that dead or devitalized teeth should be extracted if they can no longer be retained.[3]

It was only in the 1930s that an editorial appeared in the Dental Cosmos which rejected the claims of Hunter and the focal infection theory and defended the retention of pulpless teeth.

“The policy of indiscriminate extraction of all teeth in which the pulps are involved has been practiced sufficiently long to convince the most rabid hundred percenter that it is irrational and does not meet the demands of either medical or dental requirements, and much less those of the patient. Now let us turn from the destructive policy, the path of least resistance, to the constructive, even though it be beset with more difficulties, it certainly offers more possibilities of making the masticatory apparatus a useful and helpful organ rather than a crippled and constant menace to the welfare of the patient”.[2]

The rejection of Hunter’s claims laid the foundation for a more logical and conservative approach. Furthermore at this stage X-ray units were becoming available to dental practitioners which further helped to justify the retention of pulpless teeth. The introduction of X-rays was arguably the greatest leap in endodontic history. [2]

The first dental X-ray unit was adapted from a medical unit and was sold by the Victor X-ray Company in 1913, 3 years after Hunter’s lecture. A regular X-ray

machine as we know it today was not available to the dental profession until a year after the advent of the Coolidge tube in 1918. In the 1920s there were “dental X-ray studios, where a technician operated in the employ of a dentist. This was a convenience for dentists who did not have an X-ray machine and greatly helped in the diagnosis of endodontic treatment”.[4]

A further advancement in endodontics was the introduction of effective anaesthetics in the 1930s.[4] This made the invasive procedure more comfortable for patients.

Interest in endodontics grew as scientists began to research the discipline. Their efforts and simultaneous scientific findings, such as from the use of bacterial cultures, proved the safety and efficacy of root canal treatment. Thus this allowed thousands of patients to save their teeth. In February 1943 The American Association of Endodontists was founded in Chicago.[4]

In 1949, a landmark study by Zander and Glass reported the use of liquefied phenol of 90% strength directly onto exposed pulps of human teeth prior to capping the wounds with either a thick creamy paste of calcium hydroxide in water or zinc-oxide eugenol (ZOE) cement. The idea of the study was to follow, by histology, the healing pattern and any new dentine formation. Their novel approach was to extract the experimental teeth after various time periods following the initiation of the test procedures.[5] This study design, also employed by Bergenholtz and Goteborg in the same year,[6] became the norm for experimental pulpal research. Cluster effects were balanced by using two teeth in each patient by which the healing responses to both capping measures could be compared in one and the same individual. Thus began the evolution of endodontic

research, though clearly at the time there seemed to have been no ethical considerations or barriers to using human tissue for scientific investigation.

The scope of endodontics broadened to include surgical endodontics, hemi-section, intentional replantation, and endodontic implants. Biomechanical and technical, rather than mechanical instrumentation alone is now practiced and instrumentation has been simplified because of the availability of standardized instruments as well as rotary technology. Irrigation of the root canal serves several purposes not appreciated in the past. An effort is made to use mild but effective medicaments today, instead of what may have been highly irritating and caustic agents in the past e.g. EDTA has replaced the acids, and tissue-tolerant medicaments such as calcium hydroxide have replaced the phenols.[4]

1.2 Pulp and periradicular pathosis and microbiology

Chugal, Clive and Spangberg (2006) clearly opined that periapical pathosis had the strongest effect on treatment outcome.[7] Apical periodontitis occurs as a consequence of pulpal infection following various insults to the dental pulp. The major irritants of the pulpal tissue can be divided into living and non-living irritants. The living irritants are various micro organisms and viruses. The nonliving irritants are mechanical, thermal, and chemical in nature.[8]

A positive association was found between cases with endodontic signs and symptoms such as spontaneous pain, tenderness to percussion, pain on palpation, swelling and purulent exudates, and the concentration of endotoxins.[30] Black-pigmented gram-

negative bacteria in root canals of teeth with necrotic pulps have been associated with increased clinical signs.[9]

Tables 1.1 and 1.2 are after Lopez-Marcos [21] who has outlined a classification system, based on Walton and Torabinejad's classification in which he distinguished between pulpitis, necrosis, and degenerative pulp conditions.

Table 1.1: Classification of pulp pathological conditions (after Lopez-Marcos) [15]

PATHOLOGY	TYPE	SYMPTOMS	
PULPITIS	REVERSIBLE	HYPERSENSITIVITY	
	IRREVERSIBLE	*SYMPTOMATIC*	SEROUS
			PURULENT
		ASYMPTOMATIC	HYPERPLASTIC (pulp polyps)
			ULCERATED
NECROSIS	*PARTIAL*	PARTIALSYMPTOMATIC	
	TOTAL	ASYMPTOMATIC	
PULP DEGENERATION	ATROPHIC		
	CALCIFICATION- pulp stones (true/false)		
	INTERNAL DENTINE RESORPTION		
	OTHER	FATTY	
		HYALINE	
		FIBROUS	
		METAPLASTIC	
		OTHERS	

Table 1.2: Classification of periapical pathological conditions (after Lopez-Marcos).[15]

PATHOLOGY	**CONDITIONS ACCORDING TO TESTS:** Thermal, Electrical, Palpation, Percussion	
REVERSIBLE APICAL PERIODONTITIS	APICAL HYPERAEMIA	
IRREVERSIBLE APICAL PERIODONTITIS	SYMPTOMATIC	SEROUS
		PURULENT
	ASYMPTOMATIC	GRANULOMATOUS
		SUPPURATED
		APICAL OSTEONECROSIS

Bacteria in dental root canals play a decisive role in the development of chronic apical periodontitis, and their elimination is the ultimate aim of endodontic treatment of infected teeth.[10] The isolation of bacteria from endodontic infection has been limited since not all bacteria can be cultured.[11] Recent advances in molecular techniques based on direct amplification of 16S rDNA from DNA extracted from bacteria, have allowed bacterial samples to be characterized in their entirety, without the biases of culture.[12] Therefore polymerase chain reaction is a more effective, efficient and user friendly technique in evaluating the microbiology within pulp and periradicular pathosis.

1.3 Radiological features of apical periodontitis

The need for radiographs in all aspects of dental treatment has been well established. In endodontics radiographs are essential both for diagnosis and treatment decisions. Diagnostic radiology involves not only identifying the presence and nature of pathosis but also determining root and pulp anatomy and characterizing and differentiating other normal structures.

Endodontic pathoses have four distinguishing radiographic characteristics that aid in differentiating them from non-endodontic pathoses: [1]

1. Apical lamina dura is absent, having been resorbed
2. A droplet-shaped radiolucency at the apex
3. The radiolucency remains at the apex regardless of the angulation of the cone
4. A cause of pulpal necrosis is usually, but not always, evident.

Other characteristics include the widening of the periodontal ligament space and mineral loss.[13] According to Duker[14], the diagnosis of chronic periapical periodontitis can often be made simply by observing a periapical radiolucency on a radiograph. McDougal has noted that subtle osseous changes in chronic apical periodontitis can be detected radiographically.[15] Table 1.1 has been derived from many sources in order to summarize the origins of different radiographic appearances associated with pulpal pathology.

Table 1.3: The effects of different inflammatory processes on the apical tissues and the resultant radiographic appearances after inflammation of the pulp

STAGE OF INFLAMMATION	***UNDERLYING INFLAMMATORY CHANGES***	***RADIOGRAPHIC APPEARANCES***
Initial acute inflammation	Inflammatory exudates accumulate in the apical periodontal space The tooth becomes tender The patient avoids biting on the tooth	Widening of the radiolucent line of the periodontal ligament space Or No apparent changes
Initial spread of inflammation	Resorption and destruction of the apical bony socket	At apex - Loss of the radiopaque line of the lamina dura.
Continued spread of inflammation	Continued resorption and destruction of the apical alveolar bone	At apex - Area of bone loss.
Initial low-grade chronic inflammation	Minimal destruction of the apical bone. The body's defense systems lay down dense bone in the apical region	At apex - No apparent bone destruction but dense sclerotic bone evident.
Final stages of chronic inflammation	Apical bone is resorbed and destroyed and simultaneously, the body's defense systems try to confine the spread of infection by laying down dense bone around the area of resorption. Thus both processes are occurring simultaneously.	At apex - Circumscribed, well defined radiolucent area of bone loss, surrounded by sclerotic bone, periapical granuloma or cyst.

1.4 Clinical manifestations and diagnosis

Pulpal diagnosis is made on the basis of clinical signs and symptoms, diagnostic tests and a comprehensive knowledge of the reaction of the pulp to irritants. Pulpal pain symptoms occur with different intensities and these differences often aid the clinician in establishing the proper diagnosis or treatment plan and in determining whether the pulp can be salvaged. The pain process occurs mainly while tissue damage is occurring. [16]

According to Siqueira and Barnett recent clinical evidence indicates that when pain is severe, or when mild to moderate pain is present with a previous history of aching

pain in the tooth, with or without periapical radiolucency, the tooth is in the irreversible painful pulpitis category.[17] On the other hand, when clinical evidence indicates that the pain is mild to moderate with no previous history of pain, with normal pulp vitality, and there is no positive percussion sign, the pulp is in the reversible painful pulpitis category. Klausen, Halbo and Dabelsteen found that symptoms of constant pain, tenderness to temperature changes, "the tooth feels extruded", impaired mouth opening, tenderness to palpation in the apical area, and mobility, were diagnostic of irreversible pulpitis.[18]

However Seltzer, Bender and Nazimov have shown that the histopathologic status of the pulp in vital teeth cannot be determined by considering only a patient's pain symptoms. Subjective questioning of symptoms as well as clinical examination and pulp testing remain their main diagnostic regimen.[19] Various methods of pulpal evaluation do not dictate treatment but provide information that can be used with other information (history and radiographs) to establish a diagnosis. No one test in itself can be used to support a likely diagnosis. Nusstein and Beck reported that the number of days the patient had been in pain before seeking treatment was significantly greater for patients with irreversible pulpitis than for those patients with necrotic pulps.[20] According to Lopez-Marcos, a significant relationship exists between pre-endodontic and post-endodontic pain. Patients with severe preoperative pain tended to have more severe operative and postoperative pain than patients with mild or no preoperative pain.[21]

Clinical tests can be classified into peri-radicular tests, pulpal tests and tests for tooth fracture (table 1.2) can be used together with radiographs, to assist with diagnosis.

Table 1.4: Classification of endodontic tests

Pulpal tests	Peri-radicular tests	Tooth fracture test
Thermal	Percussion	White light
Electrical	Palpation	Visual
Tests cavity	Mobility	

Thermal test: this is usually made with ethyl chloride or sometimes hot gutta-percha on the tooth of concern. The tooth is isolated with a rubber dam so that the cold ethyl chloride/hot gutta percha will be confined to that tooth. When the cold/hot stimulus is used, one must try to determine if the effect of stimulus application produces a lingering effect or if the pain subsides immediately on removal of the stimulus from the tooth. The lingering quality of pain to a tooth after the stimulus is removed, is taken as evidence for irreversible pulpitis. If pain subsides immediately after the stimulus is removed, reversible pulpitis is the more likely diagnosis.

Menke and Bender stated that the application of heat has a biphasic effect. First, the initial heat application evokes a rapid, brief pain response due to the rapid fluid movement caused by sudden temperature change. As the heat application is continued, there is a period of pain cessation followed by a more intense pain. This was presumed to be due to the dilatation of blood vessels caused by heat with a transient increase in intrapulpal pressure.[22, 23]

The application of a cold stimulus to the clinical crown evokes a rapid A-delta pain response followed by an immediate pain cessation. Continuous cold application compromises the blood flow due to vasoconstriction of the blood vessels and causes anoxia, a condition under which A-delta fibers cease to function.

Selden stated that it is clinically recognized that emerging thermal sensitivity is often a sign of pulpal pathosis. The consistent scenario is the fact that the "sick" tooth will first be sensitive to a cold thermal stimulus. With a continuing pulpal deterioration, it often leads to a change in sensitivity to hot stimuli. Eventually cold will stop the heat-induced pain.[24]

Electric pulp test: this is based on the use of an electric current to stimulate the nerve fibers within the tooth thereby representing the sensation of pain. However it is important to remember that a recently erupted tooth frequently gives a false negative response. Whilst thermal stimuli evoke pain due to fluid movement in the dentinal tubules, electric stimuli evoke a pain response due to ionic movement. Electric pulp testing only excites the A-delta fibers.[25] According to Nam *et al* during electrical pulp testing, an electric current stimulates the intradental nerve fibers, which may be painful and stressful to the patient. A consistent negative response during testing indicates a necrotic pulp.[26]

Electric pulp testing has shown that there are regional differences in dentinal pain. The differences in response depend on the nerve densities located in different regions of the pulp. In areas of high nerve density, the pulpal reaction to the electric pulp tester is more severe. The lowest response threshold is present at the incisal edge or the incisal one-third facial region, followed by the mid-third region. The highest response threshold is at the cervical third.[18]

The electric pulp tester is a valuable diagnostic aid in assessing the vitality of the dental pulp but its use whilst wearing examination gloves is a controversial issue. Some believe that one should not wear examination gloves during the procedure[27] whilst others advocate the use of gloves for reasons of cross contamination and infection.[28] Kolbinson and Teplisky advocated that as long as the patient completes the circuit by holding the metallic handle of the electric pulp tester's probe, dentists can easily, reliably, and accurately use the electric pulp tester while wearing examination gloves.[29] The electric pulp tester is an excellent measure to test the vitality of an endodontically involved tooth. However the operator must ensure that the instructions for use of the pulp tester are followed accurately to ensure clarity and ease of use.

Percussion: this test is merely used to find the problem tooth. Percussion involves gentle tapping with the back of a mirror handle, on the incisal/occlusal surface of several teeth in the area in question. In one study acute apical periodontitis had the characteristic of pain to percussion, whereas chronic apical periodontitis had no pain to percussion.[23] However, another study reported no difference, [16] so clearly this test has little diagnostic value on its own and the final diagnosis requires additional information gained from other tests.

Palpation: this refers to the detection of sensitivity to finger pressure on the mucosa over the apex of a tooth, buccal or lingual, and signals the further spread of inflammation from the periodontal ligament to the periosteum overlying the bone. This examination is most effective when it can be made bilaterally at the same time.[28]

One study found that patients with necrotic pulps rated palpation pain as being more severe than did those with irreversible pulpitis.[20] However, in the absence of any other comparative studies, palpation can only be used to confirm inflammatory spread to the periosteum.

Radiographic examination: this is usually the last test, and the radiographic features of pulpitis have been discussed above.

Two clinical tests together with the radiographic examination usually provide sufficient evidence to make an informed diagnosis.[30]

1.5 Treatment

1.5.1 Introduction

The majority of patients who require root canal treatment will have been diagnosed as suffering from periradicular periodontitis.[30] A fundamental principal of treatment is the identification and removal of the causative factors in the disease process. In conventional apical periodontitis it appears that microbiological factors are the aetiological factor. With this in mind, clinical management of microbial factors should essentially be the focus of root canal therapy. Thus an essential requirement during root canal treatment is the provision of a sterile environment where further contaminating micro-organisms can be excluded from the canal. The use of rubber dam as well as sterile instrumentation is therefore essential. Rubber dam was first developed and used in the 19th century by Barnum.[31] Since then it has become

mandatory during root canal procedures because irrigation solutions have toxic effects on the soft tissue around the teeth. Furthermore optimum results are obtained for all dental procedures if the working area is protected from contamination by saliva.[32] Failure of asepsis will have a direct bearing on the outcome of treatment for the patient.

Root canal therapy comprises three actions, cleaning, shaping and obturation. Cleaning is debridement, whereas shaping is preparing the canal for obturation. Cleaning depends on proper access cavities that provide straight-line access, and requires the action of both intracanal instruments and irrigants. Files should contact and plane as many walls as possible to loosen the debris. This is followed by irrigation, which functions to flush out the debris from the canal space. Obturation of the canal depends on how well the canal is shaped as well as the condensing instruments used for obturation.[31]

1.5.2 Debridement

A recent innovation has been in the field of mechanical debridement such as the use of rotary instrumentation and systems such as Hero® Taper (Micro-Mega, Bresanton, France), NiTi (Micro-Mega, Bresanton, France) and EndoEze® (Ultradent, South Jordan, USA). Rotary instrumentation has afforded greater ease and speed of the procedure. Although one study showed that conventional hand filing with k-files was more effective in eliminating bacteria from the root canal, as compared with nickel-titanium rotary instrumentation,[33] another showed that bacteria were significantly reduced by the use of nickel-titanium rotary instrumentation.[34] Generally the shape

and rotation of rotary instrumentation is considered to be far superior in the elimination of bacteria compared with conventional hand instrumentation.[33]

Comparative studies of the various types of nickel-titanium rotary instrumentation have been published. In two studies the design of the cutting blade of the Hero system was the most effective in removing the smear layer and produced the most changes in the cross sectional area of the root canal when compared with the Profile (Dentsply/Maillefer, Ballaigues, Switzerland) and K3 (SybronEndo, Sybron Dental Specialties, California, USA) instrumentation systems.[32,35] In a different study, the Hero rotary system transported canals less and had better centering ability than the conventional stainless-steel k-files.[36]

1.5.3 Irrigation and Medication

Irrigation is an essential component in the process of treatment whereby a chemically active solution is used during instrumentation of the root canal space. Irrigation is one of the most crucial steps of canal preparation because it helps to clean those areas of the root canal system that are not directly planed by instruments.

The primary functions of an irrigant are:[37]

1. Lubrication
2. Flushing out of gross debris
3. Dissolution of organic and inorganic material
4. Antimicrobial

There are several irrigants used for intra-canal irrigation in root canal treatment. Chlorhexidene digluconate has been shown to produce sterility, improved clinical relief of symptoms, and reduced size of peri-apical lesions.[38] The efficacy of chlorhexidene and sodium hypochlorite as antibacterial agents has been shown to be similar.[39] The most commonly used and effective irrigant appears to be sodium hypochlorite solution (NaOCL). It is used in concentrations from 0.5 to 25%.[40] It has a strong bactericidal effect and is known to be an irritant to vital tissue, but if used correctly does not cause damage or interferes with wound healing. As an endodontic irrigant it has been shown to increase and improve the bonding of resin cement to radicular dentine.[41] It is also known to dissolve organic matter such as pulp tissue, bacterial tissue, necrotic pulp and bacterial products.[42] However, this method in itself cannot render canals bacteria free, as even at high concentrations it has been shown that nearly one-third of root canals remained infected after instrumentation and irrigation with NaOCL.[43] Thus it is recommended that an intra-canal medication between visits should be used to attain this goal.[41] The rationale for the use of inter-visit intra-canal medicaments is to destroy residual microorganisms and their toxins as well as to remove organic tissue.

Ideally a medicament should have the following properties: [37]

1. Destroy all root canal microorganisms
2. Have a lasting antimicrobial effect
3. Be unaffected by organic material
4. Help to remove residual organic tissue
5. Penetrate the root canal system and dentinal tubules
6. Not irritate periradicular tissues or have systemic toxicity

7. Have anodyne properties
8. Induce a calcific barrier at the junction with periradicular tissues:
9. Have no effect on the physical properties of the temporary filling material
10. Not diffuse through the temporary filling material
11. Be easily placed and removed
12. Be radio-opaque
13. Not stain the tooth.

The most common inter-treatment medication is calcium hydroxide, which has antimicrobial effects through the release of hydroxyl ions. Calcium hydroxide has been shown to dissolve necrotic tissue and enhance the tissue dissolving effects of sodium hypochlorite solution.[44] It has been shown to be effective against most root canal pathogens [44] and one study showed that large periapical lesions responded favourably enough to eliminate the need for surgical treatment.[46] Another study found that infected root canals treated with calcium hydroxide were successfully disinfected in 97% of the cases [45] and this effectiveness was confirmed when the medicament was retained in the root canal for only one week.[46] However, no bacteria-free root canals were recorded in another study, after placing calcium hydroxide for four weeks. However, the study had a small sample size, overestimated the effects of the inter-treatment medication over longer periods and used questionable sample techniques.[47,48]

1.5.4 Obturation

Obturation aims to prevent recontamination of the root canal. There are numerous techniques for obturation but there is insufficient evidence to support any particular one. The latest thermoplastic, resin-based sealer on the market is EndoRez (Ultradent, South Jordan, USA). The constituents of this material are hydrophilic and it is hypothesized [49] that the gutta percha would expand in the presence of humidity and thus reduces any voids, to produce an enhanced seal. This material was found to be most effective in sealing dentine when cured by fiber optic light.[50] However, the sealing ability of EndoRez has been questioned [50] as it exhibited the largest amount of leakage when compared with gutta percha. In another study [51] a possible reason for this leakage was thought to be the interface between the sealer and dentine. SEM views indicated that the sealer produced a sponge-like appearance at the dentine interface, suggesting that the sealer was porous and allowed leakage to occur. Further research is clearly required to assess the effectiveness of EndoRez as a root canal sealer.

The ideal root filling material should exhibit the following properties: [37]

1. It must be antimicrobial
2. It must not irritate periapical tissues but promote periapical healing
3. It must possess no systemic toxicity
4. It must have good flow characteristics
5. It must adapt well to canal walls, to the extent of being adhesive
6. It must exhibit no dimensional changes after placement

7. It must not be susceptible to disintegration by moisture and tissue fluid
8 It must be radio-opaque
9. It must have good manipulative characteristics and must be easy and quick to place
10. It must be easy to remove for post-space preparation and re-treatment if necessary
11. It must not stain dentine
12. It must be cost effective

1.6 Outcomes (Table 1.5)

Endodontic outcome is a multifactor phenomenon.[52] The success of a given therapy has been defined as “the result obtained which achieved the initial treatment goal”, and failure “a treatment that did not reach the objective or fell short of the acceptance level”. [7]The success or failure of endodontic treatment is generally thought to depend on several factors: root morphology, experience of the operator, asepsis, intracanal procedures, bacterial culturing, interpretation of radiographs, materials and techniques used, and the position of the tooth. Other factors contributing to success are periapical pathosis, the level of working length relative to the radiographic apex, and the density of obturation.[6] Chugal *et al* included preoperative pulp diagnosis, periapical diagnosis, the preoperative periapical radiolucency size, and the sex of the patient as factors contributing to endodontic treatment outcome.[53] A major biologic factor influencing the outcome is the extent of microbiological insult to the pulp and periapical tissue.[54] Recent advances in endodontics such as the introduction of rotary instruments have substantially increased the success rates. Furthermore studies indicate that when

calcium hydroxide is used as an intracanal medication over a two-visit treatment, the success rate of the treatment procedure is far superior to the one-visit treatment.[55] Another study has claimed that endodontic treatment is a predictable procedure with a high incidence of tooth retention and with the least significant number of problems.[51]

Although endodontists deal with a higher proportion of difficult cases and a smaller proportion of anterior teeth as compared with general dental practitioners, both groups of providers are noted to have comparable success rates.[56] Statistically endodontic procedures in anterior teeth are more successful than posterior teeth.[57] There was no proven difference in the success rate of endodontic treatment based on gender, position of the tooth in the arch or experience of the practitioner. [57]

Table 1.5: Factors affecting the outcome of endodontic treatment

FACTORS	OUTCOME	SOURCE
1. *MORPHOLOGY OF ROOTS* 1. *STRAIGHT ROOTS* 2. *CURVED ROOTS*	SUCCESSFUL DIFFICULT – NOT ALWAYS SUCCESSFUL	*Ingle et al, 2002* [52]
2. *EXPERIENCE OF OPERATOR*	MORE EXPERIENCE = BETTER OUTCOME	*Salehrabi, 2004* [50]
3. *ASEPSIS*	ASEPTIC CANAL = BETTER OUTCOME	*Salehrabi, 2004* [50]
4. *INTRACANAL PROCEDURES*	ROTARY = BETTER OUTCOME	*Salehrabi, 2004* [50]
5. *POSITION OF TOOTH*	EASY ACCESS ALLOWS BETTER VISIBILITY = BETTER OUTCOME	*Salehrabi, 2004* [50]
6. *INTERPRETATION OF RADIOGRAPHS*	CLEAR INTERPRETATION OF RADIOGRAPHS = GOOD DIAGNOSIS = BETTER OUTCOME	*Chugal et al, 2001* [51]
7. *BACTERIAL CULTURES*	ALLOWS THE OPERATOR TO ESTABLISH PROPER USE OF MATERIALS TO ERADICATE THE BACTERIA	*Chugal et al, 2001* [51]
8.*WORKING LENGTH*	PROPER AND ACCURATE WORKING LENGTH = BETTER OUTCOME	*Salehrabi et al, 2004* [50]
9. *OBTURATION*	GOOD TECHNIQUE = BETTER OUTCOME	*Walton, et al, 2002* [53]
10. *SEX OF PATIENT*	FEMALES = BETTER OUTCOME	*Chugal et al, 2001* [51]
11. *PERIAPICAL RADIOLUCENCY SIZE*	LARGER PERIAPICAL RADIOLUCENCY SIZE = POORER OUTCOME	*Chugal et al, 2001* [51]
12. *PERIAPICAL DIAGNOSIS*	ACCURACY IN DIAGNOSIS = BETTER OUTCOME	*Chugal et al, 2001* [51]

The validity of these data is uncertain because there are no confirmatory studies, nor reviews to substantiate them. This generally seems to be the problem with research within the scope of endodontics.

It seems self-evident that a high rate of quality outcome will be achieved from minimizing the variables that affect case adversity and by prescribing a level of treatment that is necessary to achieve success and to attain that level on a consistent

basis.[58] A completed root canal treatment should be assessed by using a proper integration of clinical and radiographic factors.[59] A longitudinal study of endodontic therapy, from 1956 to 2004, reported a success rate based on proper integration of clinical and radiographic features. The authors opined that concerns of failure regarding the need to do endodontic procedures are misguided and unsupported and that endodontic treatment should be preferred over tooth extraction and replacement procedures, including implants.[57] However this study has never been reviewed and therefore cannot be substantiated. Furthermore the clinical aspect of the study was not standardized due to varied operators. This raises serious doubt about the conclusions.

As with any other disease of infectious aetiology, prevention and treatment must be based on elimination of the etiological factor. Thus it must be reiterated, that proper shaping and irrigation is the basis of success in endodontic treatment. If the basic principles of endodontics are obeyed and observed, success can be assured in the majority of cases.

1.7 Restoration of the endodontically treated tooth

1.7.1 Introduction

Despite the historical success of endodontic treatment, a critical aspect affecting that success is the sealing of the root canal, which also affects the future functions of the tooth. Clearly, restorations that may introduce leakage will put the tooth at risk.

There is a multitude of different materials available as coronal restorations yet there is no agreement on how best to close the chamber.

1.7.2 Temporary Restoration

The lack of a coronal seal is an important factor in the development of periradicular lesions following root canal therapy. Several studies have investigated how long it takes coronal leakage to adversely affect root canal treatment once a restoration has been lost. One study reported that leakage occurred within three days after loss of the coronal restoration; [60]another indicated that it took 19 days for more than fifty percent of root canals to be contaminated and deemed a failure once the permanent coronal seal was missing.[61] The presence of a temporary restoration, such as zinc oxide eugenol, may retard the process of coronal leakage, but this protection was only temporary for a period up to 27 days after placement of this temporary seal.[62] Inadequate root canal and coronal restorations have been associated with an increased incidence of apical periodontitis.[63] It has been suggested that a permanent restoration should be placed in the most coronal portion of the access opening if there is perceived to be an extended period between completion of the root canal treatment and final restoration.[63]

With proper temporization and timely placement of the final restoration, the potential for coronal microleakage will be minimized.[64] A survey of practitioners found that most practitioners had a sound understanding of the principles involved in the restoration of endodontically treated teeth, with the possible exception of the length of time needed to establish a durable coronal seal after the placement of a root filling.[61]

1.7.3 Permanent Restorations

The quality of strength and durability of the coronal restoration determines the outcome of the endodontic procedure.[1] It has been found that composite restorations on posterior teeth were associated with more pulpal breakdown than amalgams.[65] An *in vitro* study found that glass ionomer and resin-modified glass ionomer restorative materials provided a better coronal seal against *Streptococcus mutans* than zinc oxide/eugenol in endodontic access cavities.[56] Another study found significantly more dye leakage in teeth restored with compomer compared with those filled with a resin modified ionomer.[66]

Posts are frequently used for the retention of coronal restorations. These can be custom-made or prefabricated. Few authors have investigated the coronal seal afforded by various post systems. Several new aesthetic post systems are available, but little is known about how effectively these posts seal the restored teeth. One study found that the resin-supported polyethylene fiber posts and glass fiber posts tested exhibited less microleakage compared with zirconia post systems. The latter system has exhibited a high level of leakage.[67] Another study found that roots restored with a cast post showed very little, if any, microleakage as compared with metal prefabricated posts which demonstrated the most microleakage.[68] This study further showed that the dentine-bonding cements have less microleakage than the traditional, non-dentine-bonding cements and concluded that adaptation of the post within the canal may be more important than the cement used.[66]

It has been suggested that to prevent re-infection of the root canal system, it may be preferable to restore the tooth immediately with a prefabricated post and composite system rather than place a temporary post crown and subsequently a cast post and core.[69] However the small sample size of this study makes this conclusion questionable. A longitudinal study reported a high variability in seal quality among all types of posts and cores studied and suggested that permanent cementation of the post with the coronal restoration should be carried out as soon as possible to prevent recontamination of the root canal.[70] Because neither the remaining root canal filling nor the post and core may be trusted alone for a seal, each should be performed with the greatest care and both covered with a crown as soon as possible.[71]

The root canal filling remaining after post space preparation is commonly expected to provide adequate seal. One study suggested that 3 to 6 mm remaining after post space preparation provided a coronal seal inferior to that of intact root canal fillings.[72]

1.7.4 Systemic Illnesses

Other conditions, such as systemic illnesses are assumed to further influence the outcomes of endodontic treatment. One such condition that has devastating effects on the oral environment is HIV. The oral manifestations of this condition are well researched yet there is very little, if any, knowledge on the interplay between endodontic presentation, procedural outcomes, and HIV.

CHAPTER 2: MEDICAL CONDITIONS AND MEDICAL TREATMENT REGIMES AFFECTING THE NEED FOR ENDODONTIC TREATMENT AS WELL AS THE OUTCOMES OF ENDODONTIC THERAPY

Systemic conditions such as cardiovascular diseases, diabetes, organ transplants, acute and chronic leukaemias, and HIV pose a direct challenge to endodontic therapy. The treatment of periapical lesions of various severities may cause negative reactions in such patients who may therefore require special adjustments and precautions during their endodontic procedures.

2.1 Cardiovascular disease

It is recommended that patients with ischaemic heart disease be treated in the dental chair using short appointments, using local analgesia, which may imply that endodontic treatment should preferably be done in one visit. Invasive dental procedures for patients who have had a myocardial infarct within the last six months should be deferred for three to twelve months. [73] Pulp testers should not be used during endodontic therapy in patients with cardiac pacemakers, as the pulp tester may interfere with the function of the pacemaker. The risk is small but nonetheless must be avoided.[74]

Whilst some studies have reported that endodontic treatment in patients with cardiac valvular defects can produce a bacteraemia which could lead to infective endocarditis,[75] others have shown no detectable bacteraemia following non-surgical endodontic procedures.[74] Reaming, filing and filling of the root canal seems to be

relatively safe.[74] Nonetheless the American Academy of Paediatric Dentistry recommend the use of appropriate prophylaxis prior to endodontic therapy in order to negate all possible risks.[76]

There is also a weak link concerning the relationship between the presence of endodontically treated teeth with periapical destruction and coronary heart disease, implied from a correlation found between coronary heart disease and oral infections in a longitudinal study of 447 patients.[77]

Pulp tissue samples obtained from patients with cardiovascular disease, showed vascular changes followed by reactional responses such as acute and chronic inflammatory changes, atropic and dystrophic changes, and dysphasia, all indicative of the need for endodontic therapy.[78] However this study had no control group and therefore no comparison could be made with patients who did not have cardiovascular disease.

Anatomical studies by Gafar indicate that cardiovascular and diabetic pulpal changes follow the same sequence of events.[77]

2.2 Diabetes

2.2.1 Introduction

Diabetes has been described as a complex disease with metabolic and vascular components.[79] The metabolic component involves “the elevation of blood glucose

associated with alterations in lipid protein metabolism resulting from a relative or absolute lack of insulin". The vascular component includes an "accelerated onset of non-specific atherosclerosis and a more specific microangiopathy that particularly affects the eyes and kidneys".[79] Fouad and Burlenson aptly summarised diabetes as "a chronic disease with serious health consequences".[80]

2.2.2 Endodontic treatment and diabetes

A recent review on diabetes and the dental pulp and endodontic treatment of patients with diabetes indicated that: [81]

1. There was a greater prevalence of peri-apical lesions in type 1 diabetics
2. The pulp tissue of diabetic patients may react differently from non-diabetics
3. The evidence indicated a reaffirmation of the condition referred to as "diabetic odontalgia"
4. There were trends toward increased symptomatic periradicular disease in diabetic patients who receive insulin
5. There were increased pre-operative and post-operative endodontic flare-ups in controlled diabetic patients.

The altered reaction of diabetic patients to pulpal problems may be the result of their being particularly prone to bacterial and opportunistic infections due to circulatory disorders.[81]

There appear to be differences in the natural history of endodontic infections in diabetic patients, with a significantly higher proportion of clinically severe pulpal or periodontal infections being observed.[82] There has been an association reported between the presence of diabetes and increased numbers of certain pathogenic micro-organisms in root canals.[82] The number of organisms of *P.endodontalis* and *P.gingivalis* was positively higher in diabetic patients as compared with nondiabetics. *E.faecalis* has been found to be the most prominent organism in nonhealing cases.[80] Furthermore; studies suggest that the type 1 diabetic host with no glycaemic control may experience an increase in periapical lesion size.[83] The results also showed that diabetics with preoperative periapical lesions had a significantly lower chance of success compared with non-diabetic individuals. Thus differences in the pathogenesis, progression, and healing of pulpal and periradicular pathosis in diabetics do exist.

Evidence based guidelines on antibiotic prophylaxis classify diabetes as a condition with compromised immunity, and therefore prophylactic antibiotics are advocated.[75] There was an increased risk of endodontically involved teeth showing periradular lesions but no caries, in patients with a compromised immune response, implying that a retrograde infection actually caused an endodontic response.[84] Diabetes mellitus and heart disease may predispose the host to endodontic infections in teeth that show no signs of caries.[76, 81]Endodontic infections in diabetic patients showed a more virulent microbial profile, with *Eubacterium spp* being the most prevalent, [83]indicating that the virulent microbial profile could possibly be the cause of the endodontic response.

2.3 Organ transplants

Patients with organ transplants are known to present with a high rate of infectious complications, with patients receiving renal transplants being at least risk. There is little evidence that dental disease contributes to this risk.[78]

Post-transplant infection by bacteria, viruses, or fungal organisms is the most common cause of mortality in the immunosuppressed recipient of an organ transplant. Thus it is recommended to eradicate and avoid the spread of any possible infection in the body. As such the dental practitioner who is confronted with endodontic infections must eliminate the potential sources of infection. Prophylactic antibiotics are highly recommended.[85]

2.4 The irradiated patient

The infected and inflamed periodontium can act as a focus of systemic infection especially in cancer patients. Periodontal infections can be easily overlooked because the symptoms of gingival inflammation may be minimal and the infection may be located in deeper parts of the periodontium.[86]

Endodontics and periodontics are the primary treatments of choice for the elimination of infections that threaten osteoradionecrosis in patients receiving cancercidal doses of radiation therapy for head and neck cancer. Changes have been noted in the mucosa, taste buds, salivary glands, bone, periodontium, teeth, oral flora, and muscles of mastication.[78] Endodontic treatment is performed in order to avoid extractions or to

postpone such treatment to a less threatening post irradiated period. Antibiotic cover of 500mg of penicillin, four times daily, for the entire course of endodontic treatment has been advocated.[86] The same authors opined that the tooth must never be left open for drainage in the irradiated patient and extreme care must be taken with the between-visits seal.[86]

Shorter lengths during instrumentation of the root canal are preferred over extended lengths so as to prevent periapical trauma. An ideal and safe working length is 0.5mm to 1mm short of the radiographic apex. An interesting but unsubstantiated finding went so far as to advocate that after caries debridement and endodontic therapy has been performed, the crown should be amputated at or below the gingival level and the canal should be filled with amalgam to prevent the risk of coronal leakage leading to periapical failure.[85] However this recommendation can be the cause of many other problems within the oral environment. In primary teeth, obturation with calcium hydroxide appears to be the treatment of choice.[87]

Only one study has reported on the longitudinal outcomes of endodontic therapy in an irradiated patient with leukaemia.[88] No osteoradionecrosis was seen in association with endodontically treated teeth over 54 months.[89] However, Gafar suggested that in leukaemic irradiated patients, endodontic treatment should be contraindicated because the inflammatory reactions and dystrophic changes in the pulpal tissue presented as degenerative lesions, probably because the invasive manifestation of the leukaemic process is more intense.[77]

2.5 Von Willebrand's disease

This is the most common inherited bleeding disorder in humans. It changes the platelets' physiology, thereby preventing platelet adhesion, which is required during the clotting process. It affects factor 8 of the "cascading clotting tree".[78]

Camm and Murata advocated the use of cryoprecipitate for all invasive dental procedures in order to prevent excessive bleeding. For this reason it was suggested that root canal procedures be performed as a single visit treatment.[90]

2.6 Rheumatoid arthritis

Rheumatoid disease is a chronic systemic illness. It is a common autoimmune disease of unknown aetiology.

Recent modern laboratory techniques, such as polymerase chain reaction (PCR) have helped to identify micro-organisms from the root canal in patients with arthritis. According to one review, chronic latent periradicular lesions may stimulate arthritic inflammation, because the same micro-organisms were found in both the periradicular and arthritic sites. A more convincing association was that the immunological and histological reaction occurring in the periradicular lesion was similar to the inflammatory reaction occurring in rheumatoid arthritis. IgG rheumatoid factor was found to be present in the periapical tissues of rheumatoid sufferers.[91]

2.7 HIV

The human immunodeficiency virus is predominantly transmitted via body fluids and this in itself calls for precautionary measures by the dental team. It is known that people who are HIV positive suffer from a variety of oral lesions and that these patients have a much higher level of dental and gingival disease.[92] Therefore, it may be logical to assume that endodontic infections in the HIV group would present with an exaggerated response.

Although a study reported HIV in the dental pulps of patients with AIDS, [92] a systematic review in 2002 found little to no complications in HIV positive patients receiving routine endodontic treatment, [93] and suggested that the evidence at that time was insufficient with respect to risks associated with root canal procedures in HIV positive patients. It was therefore suggested that HIV patients requiring dental treatment should be treated as for any other patient.[93] However, it is important to remember that the condition presents at different stages with increasing systemic manifestations and complications. This means that the difference in the treatment regime would be the need to modify treatment according to the presenting clinical finding or underlying systemic condition. Haematological abnormalities are relatively common with HIV infection because of the HIV disease process or as a consequence of antiretroviral drug therapy.[94,95] Lowering of the CD4 count was shown to increase the severity of haemostatic abnormalities, but this risk is most unlikely during routine non-invasive endodontics.[93]

A study on felines induced with the immuno-deficiency virus resulted in an increased prevalence of peri-apical pathosis in subjects with lowered CD4 cell counts.[96]

Because HIV is an immuno-suppressive disorder, a short-term study recommended that root canal treatment of patients who are HIV positive be performed as a one-stage treatment procedure with antibiotic cover, and that root canal treatment to molars be avoided due to a generally poor prognosis.[97] Other authors have recommended that root canal procedures for patients who are HIV positive be avoided entirely and instead extraction or surgical endodontics of teeth requiring root canal procedures be carried out.[98] But there has also been a recommendation that root canal treatment on HIV positive patients could be carried out following standard procedures and without antibiotics. [99] However this study was a cross-sectional horizontal study which ignored important variables such as CD4 counts, viral loads, and antiretroviral therapy.

With the increase in the number of HIV positive patients visiting dentists for routine and endodontic treatment, especially young patients, the need to study the reaction of HIV patients to endodontic infections and treatment becomes essential and all practitioners should have a thorough understanding of this chronic disease, which is therefore summarized in the next chapter.

CHAPTER 3: HIV

The HI virus causes a chronic, long-term debilitating illness, with no known cure. It has impacted on the world with suddenness and has sequelae of serious health, social and economic consequences.

3.1 Epidemiology

According to recent estimates from the Joint United Nations Programme on AIDS (UNAIDS), 37.8 million people world-wide were living with HIV/AIDS in 2003.[100] Of these 5.3 million were South Africans, including 230 000 children under the age of 15.[101] There are clear indications that South Africa has the highest number of people living with HIV/AIDS in the world. The mortality number caused by HIV/AIDS in South Africa, was estimated to have been 370 000 lives in 2003. This was more than 1000 people per day.[100]

The impact of the epidemic on population size is illustrated in figure 3.1, which estimates the projected population size in South Africa, with and without the AIDS epidemic. The figure shows a dramatic decrease in population in 20 years' time, especially in the 40-70 yrs age group, and especially the females in this group.[100]

This devastating epidemic has grave social and economic repercussions for South African society.

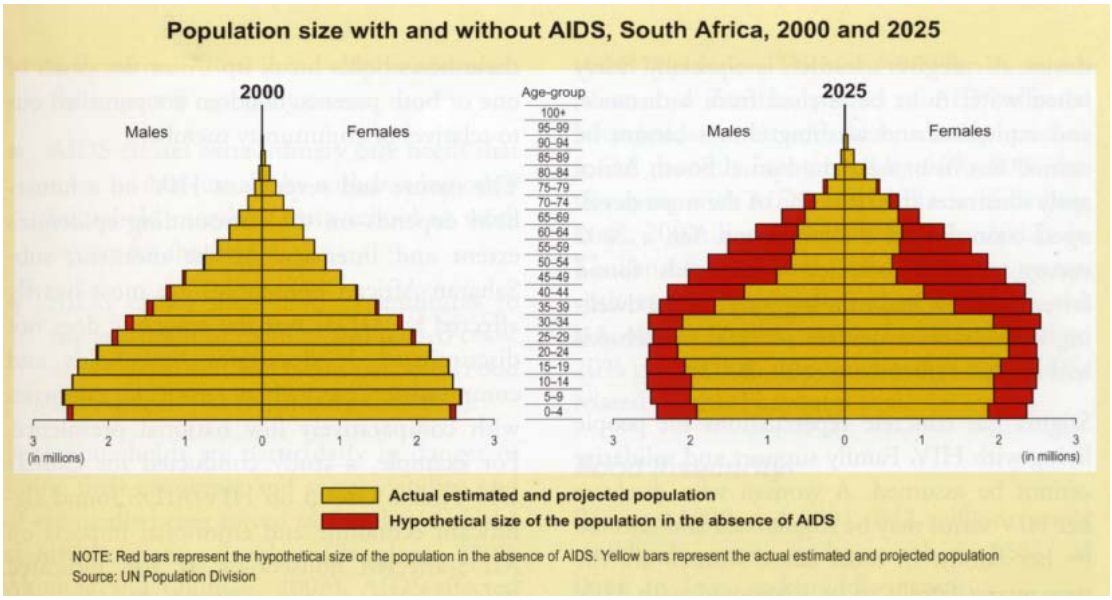

Figure 3.1- The hypothetical size of the South African population with and without AIDS (UNAIDS, 2004 Report on the global AIDS epidemic, 4th global report)[100] (used with permission).

3.2 Origins and history of the epidemic

There are two species of the human immunodeficiency virus, HIV-1 and HIV-2, but their origins are unknown. There are 3 main theories:

It is assumed that both these species arose in Africa as zoonotic infections from primate hosts. [102] These hosts have their own unique lentiviruses known as simian immunodeficiency virus (SIV). SIV is spread sexually amongst primates, but the primates themselves do not develop immunodeficiency. HIV-1 arose in Central Africa from the closely related chimpanzee lentivirus whilst HIV-2 was acquired in West Africa from the Sooty Mangabey monkey. It is thought that humans became infected when slaughtering primates for bush meat trade. According to Hunt, risk of infection

comes not so much from eating the meat but rather from the process of slaughtering the animal.[102]

Another possible origin of HIV is referred to as the CHAT theory. This theory refers to the late 1950s when a virologist called Hiliary Koprowski, created a polio vaccine called CHAT. The hypothesis is that he used monkey kidneys to grow the poliovirus needed to make the vaccine, and the HI virus leapt the species barrier to humans. This theory is supported by evidence that early cases of the HIV disease were closely correlated with places where the vaccine trials had been carried out.[103,104]

It has also been speculated that HIV was created by the American Central Intelligence Agency as a means of biological warfare. It was allegedly to be used for Black African and homosexual American genocide and Dr Robert Gallo, the person who discovered the HIV virus, was reported to be linked to a biological weapons project called MKNAOMI. This project was allegedly used to produce AIDS-like viruses in the 1970s. These allegations are based on the fact that the director of national security, Henry Kissinger, during the time of President Nixon's regime, was responsible for the MKNAOMI project. [105]

HIV was first isolated in 1983. The first populations to be affected were:

1. Men and women with multiple sex partners in East and Central Africa
2. Men who have sex with men (MSM) in some urban areas of Western Europe, America and Australia. [106]

3.3 Characteristics of HIV epidemics according to region

3.3.1 Sub-Saharan Africa

This is the most highly affected region, comprising 70% of the total HIV +ve population globally, with Botswana having the highest rate of infection in the world. The predominant mode of transmission is heterosexually;[107] the second commonest mode is mother-to-child.[108] Infection levels in women are higher than in men. A study indicated that 12 to 13 African women are infected for every 10 African men.[108]

3.3.2 Asia and the Pacific

Asia has over 16% of HIV +ve individuals globally. The predominant mode of transmission is heterosexually, with intravenous drug use also playing a significant role.[109]

3.3.3 North America, Western Europe, Australia

Initially the HIV infection mainly affected the gay, MSM population, before spreading to women and children, minority groups and the disadvantaged. Recent trends have shown increased transmission through heterosexual and intravenous drug use (IVDU).[107]

3.3.4 Eastern Europe and Central Asia

This area experienced the fastest growing HIV epidemic in recent times with IVDU being the most common mode of transmission.[107]

3.3.5 Latin America and the Caribbean

The main mode of transmission is heterosexual. IVDU and homosexuals also play a significant role.[107]

3.3.6 North Africa and the Middle East

The HIV rate in this area is currently very low. There are a few known cases and the predominant mode of transmission is IVDU. [108]

3.4 Distribution of HIV types and subtypes

HIV-1 has three groups of isolates termed:

1. M (major)
2. N (non-M, non-O)
3. O (outliers)

The majority of HIV-1 infections are caused by the M type virus. The M group is further divided into 10 genotypes, A to J. The predominant genotype in South Africa is HIV-1 subtype C.[108]

HIV-2 was first discovered in 1986 from AIDS patients in West Africa. [101] HIV-2 has five genotypes, A to E.

3.5 Basic patho-physiology

The HI virus is the virus that causes AIDS. HIV invades CD4 cells, reproduces within them, and then bursts out into the bloodstream, thereby destroying the CD4 cells. The body responds by producing more CD4 cells to ward off the infection. This immune response is ineffective because the replication of the HI virus far exceeds that of the CD4 cells, and ultimately destroys them. The cycle continues until the immune system eventually stops functioning, leaving the body defenseless against other infections.[110] This results in full-blown AIDS.

3.6 HIV in South Africa

The AIDS epidemic is one of the greatest challenges facing South Africa. It is a dynamic epidemic, which defies all barriers and exploits new opportunities for transmission. The most highly affected region in the world is Southern Africa. There is no single factor, biological or behavioral, which determines the spread of this infection.

The first two cases of AIDS were identified in South Africa in 1982. By 1999 about one-in-nine South Africans (or five million people) are living with HIV/AIDS.[111] Two-thirds of the South African youth are living with the disease, between the ages of 15-25years.[111]

South Africa, as a nation, is highly vulnerable to the impact of AIDS. It has had a devastating effect on social, economic, and, above all, human development. Factors such as the legacy of apartheid with poverty, migrant labour systems, poor education and high levels of violence and rape, create a fertile environment for the rapid spread of HIV. Coovadia and Hadingham[108] argued that as long as poverty cannot be controlled, the HIV epidemic will remain a pandemic in South Africa. They further commented that women in South Africa are at greater risk of infection due to cultural mores and an increase in domestic violence and rape. They estimated that one in four women are victims of rape or domestic violence.

Figure 3.2 demonstrates the vicious cycle of effects that HIV has on families, from a social and economic standpoint.[98] Emotional and financial burdens on AIDS orphans, make these children more vulnerable, increasing their susceptibility to the disease.

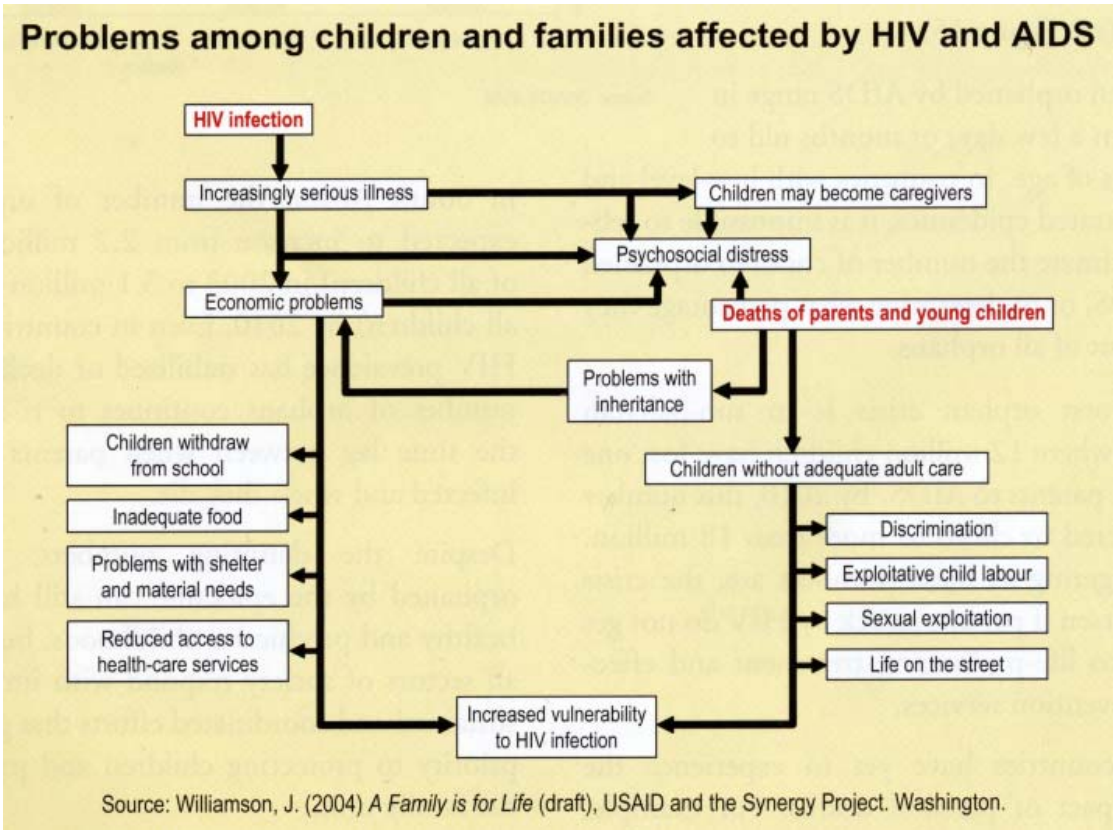

Figure 3.2: The vicious cycle amongst families and children affected by HIV and AIDS – UNAIDS, 2004 Report on the global AIDS epidemic[98] (used with permission)

3.7 WHO staging systems

Staging aims to make guidelines for clinical decision making for the management of HIV/AIDS patients. There are several classifications and staging systems for HIV, but the most commonly accepted are the Centres for Disease Control and Prevention (CDC) and the World Health Organization (WHO) classifications.

The CDC classification[109] is based on immunological parameters (CD4 counts), clinical parameters and virological parameters and requires laboratory confirmation of

many clinical events. This classification is widely used in industrialized countries that have adequate resources to support the various expensive tests required.

In developing countries, the required technology may not be available or may be too expensive to support the CDC classification system. The WHO has proposed a simplified staging system that is clinically based and flexible enough to be used in various parts of the world.[110] The WHO staging system has been proposed for use in Africa because of limited resources as well as the need for health workers at all levels to have the necessary knowledge to decide on the most appropriate patient care and support. The system is based on four groups of clinical conditions that are considered to have prognostic significance and therefore constitute stages. The clinical staging presented in table 3.1, is to be used for those who are 15 years and above and for whom there is confirmed laboratory evidence of HIV infection. A separate table is available for staging in children.[110]

Table 3.1: Revised 2005 WHO clinical staging of HIV/AIDS for adults and adolescents[110]

<table>
<tr><td colspan="2">Primary HIV infection
▪ Asymptomatic
▪ Acute retroviral syndrome</td></tr>
<tr><td>Clinical stage 1
▪ Asymptomatic
▪ Persistent generalized lymphadenopathy (PGL)</td><td>Clinical stage 2
▪ Moderate unexplained weight loss
▪ Recurrent respiratory tract infections
▪ Herpes zoster
▪ Angular cheilitis
▪ Recurrent oral ulcerations
▪ Popular puritic eruptions
▪ Seborrhoeic dermatitis
▪ Fungal nail infections of fingers</td></tr>
<tr><td colspan="2">Clinical stage 3
Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations
▪ Severe weight loss
▪ Unexplained chronic diarrhea for longer than one month
▪ Unexplained persistent fever (intermittent or consistent for longer than one month)
▪ Oral candidiasis
▪ Oral hairy leukoplakia
▪ Pulmonary tuberculosis diagnosed in the last two years
▪ Severe presumed bacterial infections
▪ Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Conditions where confirmatory diagnostic testing is necessary:
▪ Unexplained anemia and/or neutropenia and/or thrombocytopenia
▪ Extra pulmonary cryptococcosis including meningitis
▪ Disseminated non-tuberculosis mycobacteria infection
▪ Progressive multifocal leukoencephalopathy
▪ Candida of the trachea, bronchi or lungs
▪ Isosporiasis
▪ Visceral herpes simplex infection
▪ Lymphoma
▪ Visceral leishmaniasis
▪ Cryptosporidiosis
▪ Cytomegalovirus infection
▪ Invasive cervical carcinoma
▪ Any disseminated mycosis
▪ Recurrent non-typhoidal salmonella septicemia</td></tr>
<tr><td colspan="2">Clinical stage 4
Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations
▪ HIV wasting syndrome
▪ Central nervous system toxoplasmosis
▪ Oesophageal candidiasis
▪ Kaposi's sarcoma
▪ Extrapulmonary TB
▪ Pneumocystis pneumonia
▪ Recurrent severe or radiological bacterial pneumonia
▪ Chronic herpes simplex infection (for more than one month)
▪ HIV encephalopathy</td></tr>
</table>

The WHO states:

"For clinical management purposes this staging system is designed to be used:

1. as an assessment guide on when to start intervention therapy

   when to switch or stop ART

2. to assess current clinical status of individuals receiving HIV care, either on or off ART
3. encourage diagnostic testing
4. to guide clinicians in assessing the response to intervention therapy, especially where CD4 and viral load measurements are not easily available.

For surveillance purposes this staging system is designed to:

1. classify disease from least to most severe
2. be used with reference to current clinical events
3. be used in relation to previous clinical events."[110]

3.8 Oral manifestations

Oral manifestations of HIV infection are a fundamental component of disease progression and estimates of occurrence varying between 30 and 80 percent of the infected population.[111,112] Factors which predispose expression of oral lesions include CD4 counts, viral loads, xerostomia, poor oral hygiene and smoking. Oral lesions are differentiated into fungal lesions, viral lesions, bacterial infections, neoplasms such as Kaposi's sarcoma, and non-specific presentations such as aphthous ulcerations and salivary gland disease.[113]

Many initial clinical signs of HIV infection and AIDS occur in the oral cavity and may serve as markers for early immune deterioration and disease progression. Intra-oral manifestations can be recognized by clinical appearance, histological

characteristics, and causative pathogens. Their clinical appearance provides a presumptive diagnosis that in many instances is sufficient to initiate therapy.[112] However no studies thus far have managed to give exact numbers to the prevalence and incidence of oral manifestations.[114]

The common intraoral manifestations associated with HIV disease are:[112]

Fungal infections: Erythematous candidiasis, psuedomembranous candidiasis, hyperplastic candidiasis, angular cheilitis

Viral infections: Herpes simplex virus, cytomegalovirus, oral hairy leukoplakia, human papilloma virus

Bacterial infections: Necrotizing ulcerative gingivitis and periodontitis, linear gingival erythema, syphilis

Neoplasms: Kaposi's sarcoma, non-Hodgkin's lymphoma, squamous cell carcinoma

Miscellaneous: Hyper pigmentation, aphthous ulcer

3.9 Antiretroviral therapy (ART)

Antiretroviral therapy began in the late 1980s with the introduction of AZT (the nucleoside reverse transcriptase inhibitor zidovudine). The benefits of this drug were not long sustained due to the development of early resistance. In the early 1990s a combination therapy of the same class of drugs became available. The combination

therapy was shown to be much more effective than monotherapy. Even though dual therapy proved more beneficial, resistance against this combination also eventually developed.[115]

In the mid 1990s protease inhibitors (PI) and the non-nucleoside reverse transcriptase inhibitors (NNRTIs) were introduced. With the combination of these drugs viral replication could be completely suppressed. When viral replication is suppressed mutations do not occur and resistance does not develop. Thus highly active antiretroviral therapy (HAART) could be used justifiably. Since the introduction of HAART the morbidity and mortality rates amongst HIV sufferers have declined considerably.[116]

3.10 Prevention strategies

Some current HIV prevention strategies include education and awareness, blood transfusions, prevention of mother to child transmission, condom use, behavior modification and prevention of IV drug use. Future strategies include the development of HIV vaccines.[117]

The application of the ABC prevention approach to sexual behavior advocates delayed sexual debut for adolescents (A, abstinence), partner reduction (B, be faithful), and factual information regarding condom use (C, condoms). It has been successfully introduced in Uganda, a country previously experiencing significant HIV rates.[117]

3.11 Infection control

The use of proper infection control precautions to protect against transmission of bloodborne and other occupational microbial pathogens has become a routine component of health care provision.[118] Dental health care workers have a 10 times greater risk of becoming a chronic Hepatitis B carrier than the average citizen, but dentists remain at low risk for acquiring the HIV via dental treatment provisions.[119] Although it is believed that most patients report their medical histories to the practitioner to the best of their ability, it seems that many of these patients might not be aware that they carry transmissible diseases.[120] HIV and tuberculosis are increasing at a significant rate and this creates serious concerns for the health care team.

Despite the prevalence of so many serious diseases some studies have shown that not all dentists wear gloves routinely.[121] The goal of infection control is to minimize the spread of potentially pathogenic micro-organisms and to remove or to kill organisms that have contaminated objects and surfaces.[121] Emphasis must be placed on consistent adherence to the recommended infection control strategies, including the use of protective barriers and appropriate methods of sterilization or disinfection. The application of proper infection control procedures helps to protect practitioners, patients and the community.[122]

3.12 Attitudes concerning dental care

The attitudes of HIV patients in the USA, towards receiving dental care are generally quite positive. According to McCarthy, Haji and Mackie the majority of patients believed that they could trust their dentist with confidentiality, good and appropriate treatment, comfort of treatment and adequate knowledge to deal with the associated problems.[123] Patients who have been refused treatment were usually those individuals from the lower socio-economic groups who could not afford to pay.[124] Financial factors related to income and medical aid coverage have been found to limit access to, and influence use of, oral health care services by people with HIV. Many patients change providers for the fear of rejection or the refusal or reluctance of a dentist to treat.[123]

In South Africa HIV positive patients who are unemployed have free access to government health care institutions for their treatment. According to the Health Professions Council of South Africa rejection for treatment on the basis of HIV infection is considered unethical.[125] These dentists can be charged for discrimination under the Charter of Human Rights. In South Africa research involving attitudes of HIV patients as well as attitudes of practitioners towards HIV patients is lacking.[cxxviii]
It is evident that limited published scientific evidence is available to guide clinicians in regard to possible increased risks of invasive oral procedures associated with HIV status. This makes it imperative for clinicians to use their clinical judgement, to provide dental care tailored to the individual circumstances of the HIV-positive patient.

3.13 HIV and endodontics

Endodontics is an invasive procedure which is directly related to several systemic conditions.[83] As in diabetes HIV positive patients are also similarly prone to opportunistic infections due to alterations in the immune system. However the relationship between HIV and endodontics remains unclear. This research proposes to investigate this relationship to assist in the plight of the HIV patient.

CHAPTER 4: AIMS AND OBJECTIVES

4.1 Aim

To compare the presenting symptoms and the outcomes of root canal therapy between HIV positive and HIV negative endodontic patients over a 6-12 month period.

Null hypothesis

There is no difference:

1. in the presentation of pulp pathology between HIV infected patients and healthy (non-diabetic and non-HIV) controls;
2. resources used to treat endodontic lesions between HIV infected patients and healthy (non-diabetic and non-HIV) controls;
3. in the outcome of endodontic therapy between HIV infected patients and healthy (non-diabetic and non-HIV) controls;
4. between presentation of pulpal pathology, and treatment outcome and CD4 counts in HIV infected patients (non-diabetic)

4.2 Objectives

1. To compare the preoperative presentation of endodontic infections/conditions between HIV positive and negative patients, using clinical and radiographic criteria

2. To compare the presentation and outcomes of endodontic infections by HIV positive patients with their different CD4 counts
3. To identify if pulpal pathophysiology of HIV infected patients is similar to that of other systemic conditions producing an immune-compromised state.

CHAPTER 5: MATERIALS AND METHODS

5.1 Study design

The study has been carried out at the Wits Dental Hospital at Johannesburg Academic Hospital. Patients were drawn from those referred to the dental HIV clinic from the surrounding clinics in the Johannesburg area, the Wits Dental Hospital emergency clinic, as well as the Wits medical HIV clinic. The Bioethics Committee has approved this study (R14/49) (Appendix 1). Informed consent was obtained from all patients (Appendix 2).

This study was a prospective case-control clinical study. Consenting HIV infected and normal healthy controls who were diagnosed with pulpally involved teeth received endodontic treatment and were followed up at 6 months and 18 months post-operatively. One dental assistant only who is also a qualified HIV counselor, assisted the operator. The assistant pre-counseled patients and they were subsequently tested for HIV. The assistant thereafter post-counseled patients based on the outcome of their HIV test results. This allowed for strict levels of confidentiality. A single operator carried out the required procedures on all patients. The operator was blinded to the HIV status of the patients.

Calibration was done as a double-blind study. The original clinician and another independent clinician examined 20 randomly selected patient files from the study. Information according to the presenting clinical symptoms was taken into consideration and the clinicians noted the symptomatic outcomes in terms of

endodontically classifying the patient. These outcomes were recorded and statistically compared.

As part of the calibration another 10 patients were selected from the emergency section of the Wits Dental Hospital. An independent clinician ensured that all 10 patients were in need of endodontic treatment. Every patient was examined by the original clinician as well as the original independent clinician. Signs and symptoms were noted and then compared between the examiners. Once again the examinations were recorded and statistically compared.

All patients were assessed according to evaluation procedures discussed below. Thus treatment for every patient was consistent within set protocols.

5.2 Subject selection

The study group comprised 46 HIV positive patients, and the control group comprised 59 HIV-negative individuals. These groups were not matched according to gender. The age ranged between 25 to 50 years. At a probability level of 95% and a power level of 80% it was calculated that the sample size would need to be at least 45 in each group. A decision was made to try to increase the number to 60 in each group in order to maintain adequate numbers and to allow for dropouts. Certified proof from laboratory tests to confirm their HIV negative status was obtained from all members of the control group. Furthermore, the operator, who once again took a finger prick test of all participants, with their verbal consent, reconfirmed their HIV status. All patients were asked for a doctors' letter to confirm their diabetic status. All diabetic

patients were excluded from the study. Only those patients who indicated their willingness to be tested and to return for follow-up visits participated in the study. However all patients were given the dental care they required.

CD4 counts were taken of all HIV positive patients to compare the response to endodontic infection and treatment outcome according to different CD4 counts. The CD4 results were obtained from the laboratory blood tests prior to commencement of the endodontic treatment, and again at 6-monthly intervals.

5.3 Diagnostic evaluation:

A questionnaire was designed to record personal demographic information, medical history, HIV status, and standard endodontic questions of symptoms which encompassed details on the severity and duration of any symptoms including pain, swelling, and sensitivity (Appendix 3).

5.4 Clinical examination:

Clinical signs and symptoms including fever, lymphadenopathy, and malaise were noted. Full extra and intraoral examinations were performed. Extra-oral examination included signs and symptoms of jaundice, anemia, cyanosis, clubbing of the fingernails, lymphadenopathy, and oedema, as well as the presence of extra-oral swellings, asymmetry of the face, temporo-mandibular joint abnormalities, and abnormalities or discolouration of the lips and cheeks. Intraoral examination included the characteristics of swellings of various forms and sizes for example soft, hard, size, duration of swelling. It also included the examination of teeth for primary caries, restorations, secondary caries, fractures and mobility. A history of the signs and symptoms was also noted.

Clinical endodontic tests included thermal tests, percussion, palpation, and radiographs.

5.4.1 Thermal test

This test was made with ethyl chloride as well as hot Gutta Percha on the tooth of concern. The tooth was isolated with a rubber dam in order to avoid false positives from adjacent teeth. On removal of the stimulus from the tooth any lingering quality of pain was taken as evidence of irreversible pulpitis. If pain subsided immediately after the stimulus was removed, reversible pulpitis was diagnosed.

5.4.2 Percussion

Percussion provides information on the periodontal status of the tooth, whether inflamed and sensitive or normal and non-responsive. This was merely used to find the problem tooth. Percussion involved gentle tapping with the end of a mirror handle, on the incisal/occlusal surface of several teeth in the area in question. Sometimes a tooth reacted with severe pain; however the final diagnosis required additional information gained from other tests.

5.4.3 Palpation

Sensitivity to finger pressure on the mucosa over the apex of a tooth, buccal or lingual, signaled the further spread of inflammation from the periodontal ligament to the periosteum overlying the bone. This examination was most effective when it was made bilaterally at the same time.

5.5 Radiographic evaluation:

Panalipse and full mouth radiographs were taken for assessment of each patient. The panalipse was taken to eliminate any cause of pain, other than an endodontically involved tooth.

Full mouth radiographs were taken to detect peri-apical radiolucencies. These radiographs also helped to make a comparison between different teeth and what could be causing pain. The radiographic features of pulpitis are outlined in table 5.1.

5.6 Post-operative radiographic evaluation

A post-operative peri-apical radiograph was taken to assess the success or failure of the endodontic treatment rendered. Success of treatment was defined as elimination of signs and symptoms together with a decrease in the size of the peri-apical radiolucency. Failure of treatment was defined as continuing signs and symptoms together with no changes or exacerbated features radiographically.

Table 5.1: Radiographic stages of pulpitis

STAGE OF INFLAMMATION	UNDERLYING INFLAMMATORY CHANGES	RADIOGRAPHIC APPEARANCES
Initial acute inflammation	Inflammatory exudate accumulates in the apical periodontal space (swelling) The tooth becomes tender (pain) The patient avoids biting on the tooth (loss of function)	Widening of the radiolucent line of the periodontal ligament space Or No apparent changes
Initial spread of inflammation	Resorption and destruction of the apical bony socket	Loss of the radiopaque line of the lamina dura at the apex
Further spread of inflammation	Further resorption and destruction of the apical alveolar bone	Area of bone loss at the tooth apex
Initial low-grade chronic inflammation	Minimal destruction of the apical bone. The body's defense systems lay down dense bone in the apical region	No apparent bone destruction but dense sclerotic bone evident around the tooth apex
Latter stages of chronic inflammation	Apical bone is resorbed and destroyed. The body's defense systems try to confine the spread of infection by laying down dense bone around the area of resorption. Both processes are occurring simultaneously	Circumscribed, well defined radiolucent area of bone loss at the apex. Surrounded by sclerotic bone-periapical granuloma or cyst

5.7 Treatment

5.7.1 First visit

Where endodontic treatment was indicated, patients were asked to rinse with 0.2% chlorhexidene gluconate for 30 seconds.[126] Local anaesthetic was administered either in the form of local infiltration or nerve block, and rubber dam isolation of the affected tooth was performed.

All carious tissue was removed from the tooth. The root canal was approached via an access cavity preparation that was cut using standard fissure burs, round burs and endoflare burs (Micro-Mega9® Besancon, France).

The canals were irrigated using 2.5% sodium hypochlorite, and the irrigation was continued throughout the root canal treatment. The canals were cleaned, shaped and prepared using the Hero Shaper Rotary System (Micro Mega® Besancon, France), with regular irrigation throughout the procedure. The canals were dried using paper points.

The canals were obturated when the following criteria were met:

1. Tooth properly isolated to eliminate canal contamination during obturation
2. Canal system cleaned, shaped and dried
3. Absence of signs and symptoms

If these criteria were met at the first visit, then the canals were obturated using Endo-Rez® (Ultradent, South Jordan, USA) and the case was deemed a single visit therapy.

The Endorez technique used was as follows:

1. After preparation of the root canal, a master cone was fitted in the wet canal to working length in order to achieve a tug-back
2. The length of the master cone was verified with a periapical radiograph

3. The resin sealer was mixed in a double-barrel syringe and was then injected into a “skinny syringe” (Ultradent, South Jordan, USA.)
4. A suitable sized Navi-tip (Ultradent, South Jordan, USA) was selected to fit within 3mm of the working length
5. The sealer was then expressed via the skinny syringe into the canal
6. The syringe was then slowly withdrawn as the sealer was observed to fill-up the canal space
7. The master cone was then placed in the canal, with lateral condensation being used as deemed necessary.
8. Excess GP and sealer were removed 2-3mm below the CEJ with a heated instrument

If the criteria for a single visit treatment were not met, then the canal was medicated with pure calcium hydroxide (Tara Minerals, Rajastan, India) using the wipe technique and a glass ionomer material was placed temporarily until the second visit.

Glass ionomer restorative material Fuji III (GC, Japan) was used for the provisional restoration. The patient was recalled a week later, for further investigation regarding the prognosis of the completed procedure by means of radiographic and clinical parameters. The criteria included the resolution of signs and symptoms, for example no pain, no redness, no swelling in the area. Radiographic criteria included the obturation and coronal seal, as determined from postoperative radiographs.

The use of antibiotics is not routine in endodontic treatment. However, antibiotic therapy was considered only if the following cases presented: [97]

1. Pre-medication situations, for example cardiac prophylaxis
2. Non-vital pulp in a medically compromised patient
3. Non-vital pulp with an indurated, non-fluctuant swelling.
4. Post treatment swelling

5.7.2 Second visit

The patient was again assessed for signs and symptoms after one week. These were recorded. Also recorded were the duration and severity of symptoms after the first visit. If a single visit treatment had been performed, and all symptoms had been resolved, then all other oral health care treatment needs of the patient commenced. The final restoration of the endodontically treated tooth was only performed when all symptoms had subsided for at least four weeks and a waiting period of four weeks was observed. In a multi-visit case, the canals were obturated if the criteria had been met. If not, then the canals were irrigated, dried and medicated, and obturation postponed to the next visit. This information was recorded.

5.7.3 Post-treatment assessment

In order to determine if an endodontically treated tooth was deemed a radiographic and clinical success, the criteria below had to be met. The post treatment assessment and evaluation were made and noted immediately, as well as after six and eighteen months.

5.7.3.1 Criteria for radiographic success

Immediate:

1. root canal obturation should be within 1mm of the radiographic apex
2. sufficient flaring of the coronal two thirds of the canal to demonstrate proper technique
3. absence of voids in the root canal filling

Long term:

4. a decrease in the size of the initial peri-apical radiolucency.

5.7.3.2 Clinical success

An absence of symptoms such as pain, swelling, tenderness, sensitivity to thermal changes and percussion.

5.8 Statistical analysis

The statistical analysis was carried out on the advice of a statistician, and involved the construction of cross tables and testing for significant differences in the presentation

of symptoms and endodontic treatment outcomes between the two study groups. Although it was found that a proportion of the HIV +ve group of patients presented with more than one tooth requiring treatment, and all of the HIV –ve patients presented with only one involved tooth each, the analyses were made with the groups as the sampling unit. This was because the purpose of the study was to investigate the difference in presentation and treatment outcomes as a whole, and any reference to individual teeth and their analysis would have distorted the analysis in terms of the study objectives.

The following statistical tests were constructed:

- Chi-square Test of Independence for identifying statistically significant relationships between two categorical variables (one dependent and one independent variable);
- Proportional tests using z-values to identify statistically significant difference between proportions of two independent groups;
- Independent Samples T-test for identifying statistically significant differences in the averages of a continuous variable (dependent variable) between two independent groups, assuming normality in the continuous variable based on the Central Limit Theorem;
- Paired Samples Tests (Exact Tests) for identifying statistically significant differences in the averages of a continuous variable (dependent variable) between two sparse and unbalanced independent groups.

The lower limit of significant difference was set on a 95% level of confidence. SPSS for Windows (SPSS Inc., Florida, USA), a statistical software package was used for the analysis.

All relevant statistical output can be found in Appendix 4.

CHAPTER 6: RESULTS

6.1 Demography and presenting histories

One hundred and five patients consented to participate in the study; 56% were females and 44% males. Initially two patients were discovered to being HIV positive and were placed on ART.

Then 44% of the participants were HIV positive and 56% were HIV negative. Of the 45 HIV positive patients, 27 (59%) were female and 19 (41%) were male. Of the 59 HIV negative patients, 37 (63%) were female and 22 (37%) were male. The Chi-square test value ($p = 0.676$) suggests no significant differences between the two groups based on the proportional distribution by gender. The mean age of patients was 36 years in the HIV positive group and 38 years in the HIV negative group.

Table 6.1 shows the distribution of medical histories. Forty-one in the HIV negative sample presented with previous medical conditions in contrast to only 31 of the HIV positive patients. Tuberculosis was the most common condition reported amongst the HIV positive group (6 cases) and hypertension was the most common condition in the HIV negative group (3 cases). None of the medical conditions prevented the patients from coming in for the treatment.

Table 6.1: Medical histories of HIV negative and HIV positive patients

	HIV neg Frequency of condition *n = 59*	**HIV pos** Frequency of condition *n = 46*	**Total** *n = 105*
Med history			
Tuberculosis	0	6	**7**
Migraine	1	4	**4**
Hypertension on medication	3	1	**3**
Anaemia	2	0	**2**
Cancer	0	2	**2**
Heart valve	2	0	**2**
Hypertension not on medication	2	0	**2**
Asthma	0	1	**1**
Bells palsy	1	0	**1**
Eczema	1	0	**1**
Epilepsy	1	0	**1**
Gastric ulcer	1	0	**1**
Low BP	1	0	**1**
Myocardial	0	1	**1**
Pregnant	1	0	**1**
Pulmonary infection	1	0	**1**
Pleural effusion	0	1	**1**
Thyroid	1	0	**1**
None	41	31	**66**

Note: The n-values represent number of patients; some patients presented with more than one condition

Table 6.2 presents the distribution of dental histories amongst the patients. Forty-two of the HIV negative patients presented teeth with caries, whereas only three HIV positive patients presented with caries.

Table 6.2: Dental history of HIV negative and HIV positive patients

	HIV neg Frequency of condition *n = 59*	**HIV pos** Frequency of condition *n = 46*	**Total** *n = 105*
Dental history			
Caries	42	5	**47**
Clear	0	20	**20**
Bleeding gums	10	6	**16**
Crowns	2	0	**2**
Prosthetic rehab	2	11	**13**
Extractions	0	2	**2**
Braces	1	0	**1**
Broken jaw	1	0	**1**
Pericoronitis	1	0	**1**
Attrition	0	1	**1**
Broken teeth	0	1	**1**
Fluorosis	0	1	**1**

Note: The n-values represent number of patients; some patients presented with more than one condition

Table 6.3 presents the number of teeth endodontically treated. The HIV positive patients presented on average more than one tooth for endodontic treatment, whereas all HIV negative patients only presented one tooth for treatment.

Table 6.3: Number of endodontically treated teeth per patient in HIV negative and HIV positive patients

	HIV neg *n = 59*	**HIV pos** *n = 46*	**Total** *n = 105*
N umber of teeth treated per patient			
One	59	30	**89**
Two		6	**6**
Three		4	**4**
Four		1	**1**
Five		2	**2**
Six		2	**2**
Twelve		1	**1**

Note: The n-values represent number of patients

Table 6.4 shows the location of teeth treated in HIV negative and HIV positive patients.

Table 6.4: Location of teeth treated per patient in HIV negative and HIV positive patients

	HIV neg *n = 59*	HIV pos *n = 92*	Total *n = 151*
Location of teeth studied			
11	3	19	**22**
12	2	15	**17**
13	1	6	**7**
14	1		**1**
15	6		**6**
16	1		**1**
17	1		**1**
21	2	18	**20**
22		9	**9**
23	2	6	**8**
24	6	2	**8**
25	4	5	**9**
26	3		**3**
31	1	3	**4**
32	1	1	**2**
33		2	**2**
34	2		**2**
35	1		**1**
36	6		**6**
37	3		**3**
41		2	**2**
42	1	2	**3**
43		2	**2**
44	1		**1**
45	3		**3**
46	7		**7**
47	1		**1**

Note: The n-values represent number of teeth

6.2 Results regarding the study objectives

6.2.1 Preoperative presentation of endodontic infections/conditions between HIV positive and negative patients

The first study objective aimed to compare the preoperative presentation of endodontic infections/conditions between HIV positive and negative patients using clinical and radiographic criteria.

HIV positive patients with more than one tooth involved were aggregated to determine the percentage of patients with presenting signs. The results are shown in Table 6.5. None of the proportional tests (z-tests) showed significant differences in the presentation of pulp pathology between HIV infected patients and healthy (non-diabetic and non-HIV) controls. The null-hypothesis can therefore not be rejected, as there was no relationship between the presentation of pulp pathology and HIV status.

Table 6.5: Preoperative presentation of endodontic infections/conditions between HIV positive and negative patients

	HIV neg *n = 59*	**HIV pos** *n = 46*	***p-value***	***Sig.***
Presentation of pulp pathology				
Swelling	83%	80%	*0.730*	*N/s*
Periapical radiolucency	95%	87%	*0.148*	*N/s*
Palpation test	37%	35%	*0.791*	*N/s*
Percusion test	88%	87%	*0.856*	*N/s*
Cold test	71%	74%	*0.757*	*N/s*
Heat test	71%	72%	*0.950*	*N/s*

Note: The n-values represent number of patients

*** *Significant at p ≤ 0.001*

** *Significant at p ≤ 0.01*

* *Significant at p ≤ 0.05*

N/s No significance

6.2.2 Comparison of the outcomes of endodontic therapy between HIV positive and negative patients

The second research objective aimed to compare the outcomes of endodontic therapy between the two groups.

Table 6.7 shows significant differences between the HIV positive and HIV negative groups in two of the five outcomes studied, but not in the overall success rates at 18 months.

Table 6.6: Comparison of the outcomes of endodontic therapy between HIV positive and negative patients at recall

	HIV neg *n = 59*	**HIV pos** *n = 46*	***p-value***	***Sig.***
Outcome of endodontic therapy				
palpation	5%	4%	*0.860*	*N/s*
percussion	3%	17%	*0.015*	*
hot/cold	3%	15%	*0.032*	*
remaining radiographic evidence	10%	2%	*0.103*	*N/s*
overall success rate at 18 mths	78%	62%	*0.057*	*N/s*

Note: The n-values represent number of patients

*** *Significant at p ≤ 0.001*

** *Significant at p ≤ 0.01*

* *Significant at p ≤ 0.05*

N/s *No significance*

6.2.4 Comparison of the presentation and outcomes of endodontic infections by HIV positive patients with their different CD4 counts

Table 6.7 shows that no significant differences were observed in the average CD4 counts between groups that presented with positive and negative post endodontic treatment symptoms of the HIV positive group. However, the data appeared to show a trend, and at 90% probability level, there were differences in the symptoms relating to pain (palpation, percussion, hot/cold) with the patients experiencing pain having lower CD4 counts.

Table 6.7: Comparison of the presentation and outcomes of endodontic infections by HIV positive patients with their different CD4 counts

	CD4 Count			*p-value*	*Sig.*
	n	**Mean**	***SD***		
Excess bleeding					
No	*8*	439	*156*		
Yes	*38*	362	*210*	*0.181*	*N/s*
Recall palpation					
No	*44*	378	*202*		
Yes	*2*	320	*273*	*0.591*	*N/s*
Recall percussion					
No	*38*	398	*211*		
Yes	*8*	268	*110*	*0.201*	*N/s*
Recall hot/cold					
No	*39*	386	*209*		
Yes	*7*	317	*157*	*0.632*	*N/s*
Recall radiographic appearance					
Unclear	*1*	220	.		
Clear	*45*	379	*203*	*0.435*	*N/s*

Note: The n-values represent number of patients

*** *Significant at p ≤ 0.001*

** *Significant at p ≤ 0.01*

* *Significant at p ≤ 0.05*

N/s No significance

The hypothesis also considered the difference in the CD4 count before and after endodontic treatment of HIV infected patients. Table 6.9 shows that the post endodontic CD4 counts are significantly higher than CD4 counts measured prior to treatment (375 compared to 295, p = 0.000). All the patients were receiving ART throughout the course of the study.

Table 6.8: Pre and post treatment CD4 counts in HIV patients

	HIV pos *n = 46*
CD4 (Pre)	
Mean	295
SD	*183*
CD4 (Post)	
Mean	375
SD	*202*
p-value	*0.000*
Sig.	***

Note: The n-values represent number of patients

*** *Significant at p ≤ 0.001*

** *Significant at p ≤ 0.01*

* *Significant at p ≤ 0.05*

N/s No significance

CHAPTER 7: DISCUSSION

Current HIV statistics in the South African population [108] show that the average age, with the HIV positive adult population lies within the age group of 15-36 years of age, which was the case with the HIV positive group in this study. HIV statistics also show that women of all ages are more vulnerable to HIV/AIDS than men.[108]

Although symptoms of pain severity showed no statistically significant difference at a 95% confidence level between the two groups of patients, a difference was observed at a 90% level for the experience of pain classified as severe. This response could be attributed to the low immuno-compromised state of the HIV patients and to the finding that infection in the HIV positive group was more severe and involved multiple teeth. Symptoms for pulp pathology showed no statistically significant difference between HIV positive and HIV negative patients. This result was also found in a study by Zakrzewska[cxxvii], where HIV patients presented with symptoms similar to HIV negative patients.

Considerable progress has been made with respect to the use of antibiotics in endodontic patients [31]. In this study only patients presenting with swellings and severe pain were given antibiotics (penicillin) and root canal therapy was done as a two stage procedure. Shabehang [31] found that 80 to 95 percent of cultivable endodontic microorganisms remain sensitive to penicillin, supporting the use of penicillin in this study. According to Scully, Porter and Luker[cxxviii] in HIV patients, root canal therapy should be done as a one-stage procedure with antibiotic cover in symptomatic patients. Cooper [99] on the other

hand advocated that antibiotic prophylaxis is not routinely required in HIV patients undergoing root canal treatment. However, the slow healing rate, the severity of pain and lower success rates of endodontic treatment in this study support the idea that all HIV patients should receive antibiotic treatment before root canal therapy.

Length of the roots showed no difference between the two groups of patients. This can be due to the fact that root morphology has no association to the HIV status of a patient. In all cases root development had taken place before the patient contracted HIV. It may be useful to conduct studies in children in order to explore any relationship between HIV and tooth development.

The fact that oral lesions of a fungal, bacterial and viral nature occur in up to 80% of the HIV positive population, makes the oral environment more susceptible to all types of infections. Furthermore xerostomia is a common side effect of anti-retroviral therapy (ART) which can result in the activation of endogenous organisms.[128] According to a study by Fukushima *et al*,[cxxix] it seems apparent that microorganisms can reach the heart valves by a process known as anachoresis (bacterial localization) whereby the microorganisms are carried via the bloodstream to heart valves. Similarly it has been shown that in diabetic patients microorganisms are carried via the bloodstream to the dental pulp via the anachoretic process.[91] The concept of anachoresis goes back as far as 1867 when it was demonstrated that systemic bacteria were able to enter inflamed dental pulps,[cxxx] and non-carious teeth showed symptoms of requiring endodontic treatment. The process of anachoresis only occurs where there is adequate blood circulation.[cxxx]

In this study, it would appear that this process was also occurring in the HIV positive group. Although caries was common in both groups, a large number of the HIV positive patients presented with a history of no dental complications and yet required endodontic treatment. Radiographic findings further confirmed that caries was found less commonly in the symptomatic teeth in the HIV positive group compared with the HIV negative group. Radiographic caries was a very significant finding, in that in the HIV negative group (71.2%) most teeth that were endodontically involved showed radiographic caries whereas in the HIV positive group only (10.9%) of teeth that were endodontically involved showed radiographic caries.

The HIV positive patients presented mainly with single rooted teeth whereas in the HIV negative patients multi-rooted teeth were involved. Furthermore anterior teeth were endodontically involved in the HIV positive group of patients who presented with severe symptoms requiring immediate treatment. This accords with a study by Suchina *et al*, [cxxxi] where episodically treated HIV positive patients underwent five times as many anterior endodontic procedures compared with routinely treated HIV-infected patients. This would seem to imply that HIV positive patients are more susceptible to endodontic infection of multiple anterior teeth.

Excessive bleeding after preparation of the root canals occurred mainly in the HIV positive group (83%). This could be attributed to haematological abnormalities of the HIV positive patients resulting in poor healing processes.[cxxxii] Considering that all HIV

patients were on ART it could also be attributed to anemia, a side effect of the ART.[cxxxii] This finding has not been reported on before and requires further investigation.

There were statistically significant differences when the success/failure of the root canal therapy was related to symptomatic clinical presentation 18-months after treatment. On the 18-month recall visit, a high number of HIV positive patients presented with sensitivity to percussion (17%) and sensitivity to heat and cold (15%), compared with very low numbers in the HIV negative group (3%) presenting with these symptoms. This could be interpreted as being a result of the immunocompromised state of the patients, which could have influenced the rate of healing. A study by Shetty, Garcia and Leigh[cxxxiii] however found that no statistically significant differences were noted when the success of the root canal therapy was related to the symptomatic clinical presentation.

Levine[cxxxiv] found that progression of a periradicular lesion from an acute phase to a chronic phase resulted in a significant decrease in the number of CD4 cells within the periapical lesion. Although that study was done in cats, it is interesting to note that in the present study it was found that CD4 cell counts taken prior to treatment and 18-months after the completion of treatment, showed a significant increase in CD4 cell counts 18-months after endodontic treatment in the HIV patients. As all HIV patients received ART throughout the length of the study, the increase in CD4 counts could be due to the resolution of the infection. However, the healing process was still slow even though the CD4 counts increased substantially. This slow healing process could be attributed to the hypothesis that the degree of inflammation and progression of the periapical lesion was

more intense in the HIV patients as compared to the HIV negative patients. This finding calls for further research in a larger population group.

CHAPTER 8: CONCLUSIONS

Within the limitations of this study the following conclusions emerge:

5. Although the success rate was lower over the period of this study in HIV positive patients, there was no significant difference in the overall outcome in this group of patients compared with the HIV negative group. The rate is sufficiently high to warrant treatment.
6. However, patients who are HIV positive may present with more severe symptoms and during treatment more bleeding may be expected.
7. In keeping with best practice for immuno-compromised patients, it would be advantageous to put HIV positive patients on antibiotic cover during treatment.
8. The process of anachoresis may explain the high incidence of endodontic infections in teeth with no history of trauma or caries in patients who are HIV positive.

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APPENDICES

APPENDIX 1

APPENDIX 2

SUBJECT INFORMATION FORM

Hello, name is Dr. S Tootla from the Restorative Dentistry Department. I am doing a research study on root canal treatments (removal of the infected nerve within the tooth) comparing patients who have been infected with the human immunodeficiency virus (HIV), who are referred to as seropositive and those who are not infected, referred to as seronegative. I would like to inform you about this study and invite you to participate. You may decide whether you are willing to take part or not.

In order to compare the seropositive with the seronegative group, we will need to perform an HIV test on you after an appropriate counseling. This entails taking a small sample of blood (Approximately one tablespoon), which will be sent to a laboratory for testing. Your test results will be kept confidential. If you have already been tested, we request your permission to check your results. Irrespective of your HIV status, you will be allowed to participate in this study. HIV is very common in South Africa. The rate of endodontic lesions (infected area) is higher in seropositive individuals compared to seronegative individuals. The chances of developing this infection can be reduced by improving the general Oral Health status of the individual after appropriate education. Antibiotic treatment may also be necessary. This study will help in defining other ways of preventing and managing this problem.

In order to understand this study, I would like to examine your mouth, take an X-Ray of the appropriate tooth/teeth, explain to you how to brush your teeth correctly and give you a toothbrush and toothpaste. Furthermore, antibiotic therapy will be prescribed. You will be asked to return after one week when another X-Ray will be taken, and endodontic treatment (removal of the infected nerve) will commence to completion. At this stage a paper point will be used to take a bacterial sample the root canal space. This sample will be transported to the Microbiology Laboratory. This will allow us to determine the type of infection present. You will then be asked to return after one month and three months consecutively when further X-Rays and examinations of the root canal treated tooth will proceed. I will be present at every visit in order to explain your treatment and progress, and conduct the treatment. You will be asked to visit our clinic for four appointments. At these visits, a clinical examination and intra-oral X-Rays (X-Rays of the specific tooth/teeth) will be done, together with the required endodontic procedure. The healing rate of the endodontic lesion and treatment will be documented and compared in the seropositive and seronegative individuals.

The endodontic treatment should not cause pain or harm you in any way. Rather it should help to alleviate any pain or associated discomfort that may have been present in the involved tooth/teeth.

Participation in this study is entirely voluntary. Refusal to participate will not affect your required dental treatment in any way. You may discontinue or withdraw at any stage or time during the study, without prejudice to the treatment you are receiving. If you have any queries or questions with regard to this study, kindly contact me at the following

number 072 2318185. If you are willing to participate in the study, please read and sign the informed consent form.

INFORMED CONSENT FORM

The aims and procedure or the study that I have been to take part in have been explained to me by ……
I have had the opportunity to ask questions and to consider the answers given. I understand that participation in this study is entirely voluntary.
I understand that I can withdraw from the study at any time, should that be necessary.

I hereby freely give my informed consent to take part in this study.

NAME OF PATIENT:…… DATE:……..

SIGNATURE:…….

I confirm that I have explained the nature of the above study to the above named patient.

NAME OF DENTIST:……. DATE:……

SIGNATURE:……...

1……. DATE…….
WITNESS

2……. DATE……..
WITNESS

AFFIDAVIT FOR HIV TESTING

I,……. hereby confirm that

Dr…… has discussed HIV infection with me, including its implications and its possible complications on my life.

I understand that testing is voluntary, and I give permission to have my blood tested for HIV

OR

I have already been tested for HIV. I give permission to Dr. Saidah Tootla to check my results.

SIGNATURE OF PATIENT:……
DATE:…….

SIGNATURE OF DENTIST:……
DATE:…….

SIGNATURE OF WITNESS:……...
DATE:……..

APPENDIX 3

No	
Date of Birth	Age:
ID Number	
Home Add	
	Code:
Postal Add	
	Code:
Tel: Home	Work:
Cell Number	
Bussiness: Company	
Address	
Occupation	
Medical Aid	
Medical Aid Number	
Medical Doctor	
Regular clinic/hospital	Tel:
Emerg contact person	Tel:

Medical History		
Dental History		
H status		
CD4 counts	Date:	Count:
	Date:	Count:
	Date:	Count:
	Date:	Count:
	Date:	Count:
Extraoral exam		
Swelling		
Facial asymmetry		
TMJ		
Muscles of Mastc		

ENDODONTIC DATA PAIN HISTORY	
Pain History	
Date of onset of sympt	
Severity	
Heat/Cold/Sweet	
Spontaneous pain	
Awake at night	
Pain on chewing	
Discription of pain	Dull
	Sharp
	Throbbing

SIGNS OF INFECTION	
Swelling	
Size of swelling	
Nature of swelling	Soft: Hard:
Anatomical Position	
Duration of swelling	
Temperature	
Sinus tract	
Drainage	
Lymph adenopathy	

GENERAL CONDITIONS OF MOUTH	
Dental status	
Periodontal condition	
Oral hygiene status	
Occlusion	

AFFECTED TOOTH: TOOTH NUMBER	
Caries	
Restoration	
Pulp involvement	
Trauma	
Restorability/Prognosis	
Occlusal status	
Perio-Endo lesion	
Pocket depths	
Furcation involvement	
Periodontal prognosis	

ENDODONTIC TESTS	
Percussion test	
Mobility test	
Cold test	
Heat test	
Tooth Fracture Test	

RADIOGRAPHIC FINDINGS	
Caries	
Restoration	
Periradicular lesion	
Furcation lesion	
Pulp space	
Chamber anatomy	
Calcifications	
Number of canals	
Canals sclerozed/patent	
Root Morphology	
Curvature	
Length of roots	

DIAGNOSIS	
Normal pulp	
Reversible pulpitis	
Irreversible Pulpitis	
Necrotic pulp	
Peri-radicular	
Perio-endo lesion	
Previous Endo treatment	

WORK RECORD

FIRST VISIT TREATMENT	
Caries removal	
Access cavity	
PP swab for PCR	
Pulp removal	
Canals explored	
Canal medication	
Temporary seal	
Antibiotics	

TIME TAKEN FOR PROCEDURE:……..MINS	
MATERIALS USED	AMOUNT
Local anaesthetic	
Rubber dam	
Burs	
Irrigating solutions	
Medicaments	
Temporary seal	
Files	
X-Rays	
GP	
Sealant	

SECOND VISIT	
Symptoms	
Time symptoms	
Swelling	
Sinus tract	
Mobility	
Percussion test	

TREATMENT	
Caries removal	
Access cavity	
PP swab for PCR	
Pulp removal	
Canal medication	
Temporary seal	
Antibiotics	
Time for procedure	

MATERIALS	AMOUNT OF MATERIAL
Local anaesthetic	
Rubber dam	
Burs	
Irrigating solutions	
Medicaments	
Temporary seal	
Files	
X-Rays	
GP	
Sealant	

OBTURATION RECORD	
Canal	WL Size Taper