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Front Cover:
Top: Complicated crown fractures of central incisors.
Middle: Deep caries in an immature permanent molar.
Bottom: Complicated crown fracture of an erupting, immature right central permanent incisor.
Editorial Notices

The New Zealand Endodontic Journal is published twice yearly and sent free to members of the New Zealand Society of Endodontics (Inc). The subscription rates for membership of the Society are $35 per annum in New Zealand or $45 plus postage for overseas members. Graduates of the University of Otago School of Dentistry enjoy complimentary membership for the first year after graduation. Subscription inquiries should be sent to the Honorary Secretary, Dr Mike Jameson, 2 Granville Terrace, Dunedin.

Contributions for inclusion in the Journal should be sent to the Editor, Tina Hauman, PO Box 647, Dunedin. Deadline for inclusion in the May or November issue is the first day of the preceding month.

All expressions of opinion and statements of fact are published on the authority of the writer under whose name they appear and are not necessarily those of the New Zealand Society of Endodontics, the Editor or any of the Scientific Advisers.

Information for Authors

The Editor welcomes original articles, review articles, case reports, views and comments, correspondence, announcements and news items. The Editor reserves the right to edit contributions to ensure conciseness, clarity and consistency to the style of the Journal. Contributions will normally be subjected to peer review.

It is the wish of the Editor to encourage practitioners and others to submit material for publication. Assistance with word processing and photographic and graphic art production will be available to authors.

Arrangement

Articles should be typewritten on one side of A4 paper with double spacing and 3cm margins. The author’s name should appear under the title and name and postal address at the end of the article. If possible, the manuscript should also be submitted on computer disc, either Macintosh or PC compatible.

References

References cited in the text should be placed in parenthesis stating the authors’ names and date, eg (Sundqvist & Reuterving 1980). At the end of the article references should be listed alphabetically giving surnames and initials of all authors, the year, the full title of the article, name of periodical, volume number and page numbers.

The form of reference to a journal article is:

The form of reference to a book is:

Illustrations

Illustrations should be submitted as clear drawings, black & white or colour photographs and be preferably of column width. Radiographs are acceptable. However a black & white photograph is preferred. Illustrations must be numbered to match the text and bear the author’s name and an indication of the top edge on the back. Legends are required for all illustrations and should be typewritten on a separate page.
President’s Report

It is hard to believe that another year is almost over. It has been a busy time, I am sure, for most people, and a break over the summer will be well earned.

May I start by thanking our past president Dr Peter Cathro for all the hard work he has done on behalf of the society over the years and also for the profession of endodontics. Peter is now slowly becoming an Oz, but I am sure he will not forget his true home. Thank you so much Peter, we are fortunate indeed to have such a great ambassador over the ditch.

Peter has passed the job of editor of the journal on to Dr Tina Hauman. It is a lot of work and the society is very grateful to Tina for taking on this task.

There is now a new Endodontic Society committee made up of both specialist and general dentists. The new secretary is Dr Mike Jameson and the treasurer is Dr Deborah Creagh. Many thanks to Hani Naoum, Craig Waterhouse, Robyn Cameron, James Fairhall and Phillip Chong, who have put their hands up to be on the committee. We have had one joint meeting and a teleconference, both of which went well. Thank you to all the committee members for giving up their precious spare time to be available for this.

I would like to congratulate, on behalf of the society, this year’s new endodontic graduates, Jack Lin, Darryl Violich, Rajneesh Roy and Dikesh Parmar. Well done, guys! It’s hard work and at times a long slog, but I am sure all your efforts will be rewarded. Welcome also to the current team of postgraduates, Artika Patel, Abdul Azizz and Shalin Desai.

The big news is that we are currently in the throws of organising with our Australian colleagues a joint endodontic meeting in Tasmania for next year. The date is 20-22 November 2008 in Hobart. So mark it in your dairies and start booking your tickets now because it is going to be great. We have speakers from Australia and New Zealand, along with a couple of well-known names from further afield. We really hope that you can make it. It’s the first time that we have joined forces, and if it’s a success we hope to make it a regular event.

Thanks again to all our members. If there is anything you would like brought up at our next committee meeting, please feel free to contact either Mike or myself. Remember it is your society.

Here’s looking forward to a great 2008.

Sara Jardine
Editorial

I wish to add to Sara’s report by thanking Peter for his commitment, amongst his many other roles, in editing this journal and for gently easing me into the role. Best wishes to your family and you for a very happy future in Adelaide.

I am also very grateful to the postgraduates for their contributions in the form of assignments and case reports. At the same time, I wish to invite you, the members, to share those interesting cases you see in your practices with your colleagues – remember this is your journal and editorial support will be happily given.

The major objective of endodontics is to prevent or eliminate apical periodontitis. The most efficient way is prevention in the form of maintaining a vital pulp. Rajneesh’s assignment on vital pulp therapy revisits this very important part of endodontics.

Artika discusses the role of viruses in endodontics. Viruses are not normally a consideration in our management of endodontic infections, but this assignment emphasises the need to include viruses in our differential diagnosis of pulp and periapical infections.

I wish you all a very happy and successful 2008.

Tina Hauman
Vital Pulp Therapy
Rajneesh Roy

Introduction
Vital pulp therapy is broadly defined as dental treatment undertaken to minimize trauma to the pulp. It also involves the stimulation of tertiary dentine matrix formation in and by vital dental pulps. Materials or agents used for this purpose may be non-biologic, or biologic (Rutherford & Fitzgerald 1995). Vital pulp therapy was first used in 1756 by Phillip Pfaff. He packed a small piece of gold foil over an exposed pulp to promote healing (Glass & Zander 1949). Since then hundreds of investigations have been directed towards maintenance of the vitality of an exposed pulp.

The dental pulp
The dental pulp is a highly vascular connective tissue located within the pulp space of the tooth. It performs several important functions such as the formation of dentine, tooth sensitivity, nutrition and defence (Leeson et al. 1988). Since a vital, functioning pulp is capable of initiating defence mechanisms to protect itself from bacterial invasion, it is preferable to preserve the vitality of an exposed pulp and keep it free of inflammation.

Structure of pulp
The pulp consists of four distinct zones, namely, the odontoblastic layer at the periphery, a cell-free zone, a cell-rich zone and the core, consisting of the major vessels and nerves. Odontoblasts, fibroblasts, undifferentiated mesenchymal cells, macrophages and other immunocompetent cells are the major cell populations found in the pulp. The odontoblasts form a single layer, lining the periphery of the pulp, and have processes extending into the dentine (Ten Cate 1994).

Mechanism of wound healing in the pulp
The sequence of reactions observed in a pulp exposure is similar to that seen when connective tissue is wounded. There are four phases in healing- haemostasis, inflammation, proliferation and remodelling. These phases overlap as wound healing is a continuous process (Gottrup & Andreasen 1994). Initially, the tissue adjacent to the exposure is characterised by the presence of some necrotic tissue, inflammatory cells and extravasated erythrocytes. There is an exudation of fibrinogen and blood coagulation after the injury and the acute response is dominated by neutrophils. Pro-inflammatory cytokines are released in response to both trauma and bacterial infection and alter vascular permeability. Chemotactic signals prompt adhesion molecule interactions between leucocytes and endothelium thus, enabling transmigration of inflammatory cells (Albedla et al. 1994).

The role of calcium hydroxide
Calcium hydroxide-containing agents were first used in 1930 and have been used widely since (Hermann 1930). Studies have shown it to be extremely toxic to cells in tissue culture. This has prompted the search for a formula that would stimulate dentinal bridge formation without sacrificing any pulp tissue (Negm et al. 1981, Stanley & Pameijer 1985).

The exact mechanism of action of calcium hydroxide is not known, but its high pH (11-13) is considered a factor. On application, it releases hydroxyl ions, followed by lytic and coagulation necrosis on the surface of the pulpal wound. This necrotic tissue forms a membrane, with the inflammatory and reparative processes occurring underneath. The beneficial effect of calcium hydroxide is twofold, bactericidal and irritation of pulp tissue, thus stimulating the pulp to defence and repair (Schroder 1985). Calcium hydroxide also induces apoptosis in the pulp (Goldberg et al. 1994). Apoptosis is a non-inflammatory controlled, cell death mechanism. It is different from necrosis which is pro-inflammatory (Lovschall & Mosekilde 1997).

The role of mineral trioxide aggregate (MTA)
MTA has become the recommended material to use in contact with vital pulp tissue to promote
healing (Nair et al. 2007). Used as a pulp capping agent in animal studies, MTA was shown to result in a higher frequency of calcific bridge formation with less pulpal inflammation compared to calcium hydroxide (Abedi et al. 1996, Pitt Ford et al. 1996). More recent studies confirmed the ability of MTA to stimulate reparative dentine after mechanical pulp exposure in animals (Tzafias et al. 2002, Faraco et al. 2001) and in human teeth (Acinehchi et al. 2003, Caicedo et al. 2006, Farsi et al. 2006).

The ability of MTA to induce hard tissue formation may be due to the material’s excellent sealing ability, its biocompatibility and its alkalinity. An in vitro investigation demonstrated that MTA is able to stimulate cytokine release from bone cells suggesting that it actively promotes hard tissue formation rather than being inert (Koh et al. 1995, 1997, 1998). It also allows the attachment of osteoblasts in the form of a monolayer (Zhu et al. 2000). However, some studies suggest that it is only osteoconductive and not osteoinductive (Moretton 2000).

Reparative dentine formation
The healing of pulpo-dentinal defects requires migration of granulation tissue, originating from central pulp sites, and differentiation of a new generation of odontoblast like-cells. The precursor cells are probably derived from undifferentiated mesenchymal cells of the cell-rich subodontoblastic layer. Other cell populations, such as perivascular cells and bone marrow stem cells, migrating via the bloodstream, have also been proposed as possible progenitor cells (Tziafas 1997). Fitzgerald and colleagues (1990) studied migration and proliferation in monkeys after capping with calcium hydroxide. They observed a continuous influx of newly differentiating odontoblast-like cells at the material-pulp interface. At least two replications of DNA are required after pulp capping before cell migration occurs with differentiation into odontoblast-like cells (Fitzgerald et al. 1990).

Reparative dentinogenesis involves a complex sequence of biological processes. The initial precipitation of minerals is associated with the detection of mineral vesicles (Hayashi 1982). Dentinal bridge formation can be seen after 1 month around the site of trauma, representing a defensive interface between the necrotic zone and the new odontoblast layer. Microscopic examination reveals that 89% of dentinal bridges contain ‘tunnel defects’ that leave the pulp prone to bacterial infection (Cox et al. 1996).

Effect of Caries on Dental Tissues
Early carious lesions in enamel are characterised by subsurface demineralisation from acids produced by plaque bacteria. Bacterial colonisation of enamel occurs after breakdown of the surface layer, which is highly mineralised. There is some disagreement as to when the first pulp-dentine complex reactions occur. In 1965 researchers found an increase in chronic inflammatory cells beneath lesions confined to enamel (Brännstrom & Lind 1965). Another reported that this occurred only when caries extended into dentine (Massler 1967).

At the advancing front of a dentinal lesion, demineralisation precedes bacterial invasion. Bacterial acids and products diffuse ahead of the bacteria towards the pulp. The concentration of bacteria, the permeability of the dentine and the pulpal fluid pressure influence the rate at which this occurs (Kim & Trowbridge 1998).

In the case of occlusal caries, bacterial infection of the dentine occurs only when caries extends into the middle third of dentine and becomes radiographically visible (Ricketts et al. 1995).

If caries continues unchecked, the odontoblastic layer exhibits degenerative changes before inflammatory changes become apparent within the pulp (Trowbridge 1981). Dead odontoblasts are replaced by odontoprogenitor cells from the cell-rich layer. Undifferentiated mesenchymal cells differentiate into odontoblast-like cells and produce reparative dentine. The character of reparative dentine depends upon the severity of the caries. In aggressive carious lesions, it is irregular with cellular inclusions but in slow progressing lesions it can resemble normal tubular dentine. A healthy pulp is required for the initiation of defensive reactions (Ricketts 2001).

It is generally assumed that the proximity of the untreated carious lesion to the pulp is indicative of the severity of pulpal inflammation (Reeves & Stanley 1966). According to Shovelton (1968) hyperaemia and pulpitis are initiated when caries advances to within 0.25-0.3 mm of the pulp. However, pulp inflammation can only be reliably diagnosed by means of histology.
Vital Pulp Therapy

The specific location of caries on the tooth is an important factor in the final effect. Smooth surface lesions are present in an open environment. The slow-progressing nature of caries at these sites can be attributed to fewer protected niches for bacteria in these sites while a closed ecosystem develops in occlusal as well as proximal lesions with more aggressive progression of the lesion (Edwardsson 1987).

Vital Pulp Therapy of Permanent Teeth

It has been shown that the absence of infection is the key factor in pulpal healing after exposure (Kakehashi et al. 1965). Failure is, therefore, a result of infection either due to remaining bacteria or new infection from leakage. The outcome of therapy also depends on the pre-treatment inflammatory status of the pulp (Ørstavik & Pitt Ford 1998b). Capping of inflamed pulps has an inferior success rate (Tronstad & Mjör 1972, Mjör & Tronstad 1974).

Control of haemorrhage and the capping material also influence success rates (Matsuo et al. 1996). Many materials and methods have been used for pulpal haemostasis, such as sterile cotton pellets with pressure, with or without saline, hydrogen peroxide, sodium hypochlorite, chlorhexidine etc (Pameijer & Stanley 1998, Hafez et al. 2002). Ferric sulphate causes substantial clotting which may be deleterious to success, so the use of this agent is not encouraged (Stanley 1989).

Several studies have demonstrated the value of sodium hypochlorite as a haemostatic agent in pulpotomies (Hafez et al. 2002, Sen Tunc et al. 2006, Vargas et al. 2006). Hafez and colleagues placed a cotton pellet soaked in 3% sodium hypochlorite for 30-50 seconds on the exposed pulp and afterwards rinsed the cavity with sterile water. In most cases, all haemorrhage had stopped without the presence of a clot (Hafez et al. 2002).

If haemorrhage persisted, they repeated this for another 20 seconds. Vargas and co-workers used sodium hypochlorite as a pulpotomy medicament for primary teeth. It was shown to be a better alternative to ferric sulphate (Vargas et al. 2006).

Techniques

Commonly used vital pulp therapy techniques for permanent teeth are direct and indirect pulp capping and complete and partial pulpotomy.

Direct pulp capping refers to the placement of a protective dressing or cement directly on the exposed pulp. Indications for direct capping include teeth traumatised within the last 24 hours, or iatrogenic pulp exposures during cavity preparation. Longstanding exposures that have been exposed to the oral bacterial flora and are inflamed are not ideal candidates for capping (Mass et al. 1995).

A retrospective study of direct pulp capping with calcium hydroxide-containing compounds showed no statistical difference in clinical success between caps following small exposures due to trauma from cavity preparation or perforation due to excavation of carious dentine in teeth with no preoperative pain. The survival rate of 97% after one year was reduced to 82% after five years. This reduction was attributed to subsequent operative procedures and new carious lesions (Hørsted et al. 1985).

Direct pulp capping of young permanent teeth is expected to be more successful because the pulpal tissue is more reactive than in older teeth which have more fibrous pulps. Some studies have supported this assumption, whereas others have failed to show a negative correlation between the age of the tooth and the success of pulp capping (Haskell et al. 1978, Baume & Holz 1981).

Capping materials

Recently, materials like hydroxyapatite, tricalcium phosphate, mineral trioxide aggregate (MTA), osteogenic protein and dentine bonding materials have been used.

MTA shows much promise. It is similar in composition to Portland cement and sets hard in moist environments. It releases calcium hydroxide during the setting reaction. Animal studies have shown good sealing ability and hard tissue inducing capacity (Faraco & Holland 2001).

Dentine bonding materials have also shown hard tissue formation in animal studies (Cox et al. 1998). Their use is based on the theory that if pulp tissue can be protected from bacterial contamination, healing would ensue. Clinical and radiographic studies in humans have shown positive responses to vitality testing and absence of pain following capping with dentine bonding materials (Pereira et al. 2000). However, histological studies in
humans have shown lower success rates with
dentine bonding materials than with calcium
hydroxide (de Souza et al. 2001).

The research community remains divided on the
subject of resin pulp capping. Some studies have
shown calcium hydroxide capping to be far more
successful than resin pulp capping (Pameijer
& Stanley 1998, de Souza et al. 2001). Other
studies have shown that some resin adhesives
provide better results than others, suggesting that
pulp capping success may be material dependent
(Tsuneda et al. 1995, Kitasako et al. 2002).

Other factors may influence the results of pulp
capping studies as different studies have reported
varying results with a single material. One example
of this is the self-etching resin adhesive system
Clearfil Liner Bond II (Kuraray, Osaka, Japan).
Its success relative to calcium hydroxide has been
reported as much less, somewhat less, or nearly
the same in different studies (do Nascimento et al.
2000, Kitasako et al. 2000, De Marco et al. 2001,

The presence of dentine chips in the pulp from
burs is unavoidable. Controversy exists as to
whether these promote or retard healing (Stanley
1989). Some researchers feel that dentine chips
promote bridge formation (Stanley 1998). Other
researchers describe them as sites for focal
infection and abscess formation (Kalnins &
Frisbie 1960).

**Indirect pulp therapy**

In teeth with deep carious lesions without any
clinical evidence of pulpal degeneration or
periapical pathology, excavation of the caries
can be stopped at stained, but firm dentine in an
attempt to avoid exposure (Kidd & Smith 1996).
The remaining bacterial numbers in the carious
dentine left behind are diminished by calcium
hydroxide or zinc oxide-eugenol used as dressing
(Fairbourn et al. 1980).

The carious dentine is either sealed under a
permanent restoration, or a two-step approach
is used (Leskell et al. 1994). The cavity is re-
entered after a period of time and the degree of
remineralisation tested and any soft residual
dentine removed. Bjørndal and colleagues (1997)
investigated 31 grossly carious teeth with staged
caries removal over two separate appointments
6-12 months apart. At the first appointment, the
periphery was rendered caries-free but soft, wet
dentine was left pulpally. A calcium hydroxide
dressing was placed and the tooth restored with
glass ionomer cement. At the second visit, cavities
were re-entered. The dentine was found to be
darker, harder and drier (Bjørndal et al. 1997).
The difficulty with a single stage procedure is
to determine when to stop excavation. There are
two further disadvantages of the single-stage
procedure. Firstly, on remineralisation, the carious
dentine dries out, leading to a reduction in volume,
causing voids under the restoration. Secondly,
if the restoration is lost, the dormant lesion can
potentially reactivate and progress rapidly.

**Partial pulpotomy**

Partial pulpotomy (Cvek pulpotomy) refers to
removal of pulp tissue to the level of healthy
coronal pulp (Cvek 1978). This procedure is
based on the assumption that if the inflamed tissue
is removed, the healthy underlying tissue is likely
to remain healthy and form a hard tissue bridge
over the wound site.

A sterile, high-speed diamond bur under copious
water spray is used to excise inflamed pulp tissue.
The excision is considered complete when the
stump stops bleeding excessively. The wound is
irrigated with saline until haemostasis is achieved
and is covered with calcium hydroxide. Calcium
hydroxide stimulates dentinal bridge formation
which gives the underlying pulp something to
attach to. Dentinal bridges contain tunnels and
porosity due to cellular inclusions and empty
vascular spaces. The degree of trauma to the
pulp determines the permeability of the dentinal
bridge. Despite the presence of porosity in the
dentinal bridges, it does provide a physical barrier
for pulpal protection. MTA may be used to replace
calcium hydroxide in these treatments.

**Full coronal pulpotomy**

This procedure varies from partial pulpotomy
in that it involves the complete removal of the
coronal pulp followed by the placement of a
wound dressing at the canal orifices. A number
of chemical compounds with varying toxicity
have been used as dressings. Phenol, creosote and
formaldehyde have been used as pulp mummifying
agents (Ørstavik & Pitt Ford 1998a). As the short-
term success-rate for this procedure is good, it is
used widely for primary teeth.

Although the use of formocresol in permanent
teeth with pulp exposures has been advocated in the past (Rothman 1977), there are various disadvantages. Fuks and colleagues (1983) found a high incidence of internal resorption in monkey teeth. Rolling and colleagues found that the portion of the canal apical to formocresol application was very tortuous and hard to instrument if endodontic treatment is needed years later (Rolling et al. 1976).

A study involving 26 permanent molar teeth with carious pulp exposures and radiographic periapical lesions has shown that full coronal pulpotomy and capping with calcium hydroxide resulted in clinical and radiographic success in 24 teeth (Caliskan 1995).

Vital Pulp Therapy for the Immature Permanent Tooth
Pulpectomy and endodontic treatment in immature permanent teeth arrests physiologic dentine formation, resulting in a root with thin walls and predisposition to fracture (Camp 1998). Hence, in an immature permanent tooth with carious exposure, it is worthwhile to consider a clinical technique that preserves as much pulp tissue as possible to enable continued dentine deposition and root development.

The techniques of complete and partial pulpotomy enjoy good success rates in immature permanent teeth.

Mejare and Cvek (1993) performed partial pulpotomies on thirty seven young posterior teeth with deep carious lesions and exposed pulps. Thirty one of these teeth had no clinical or radiographic signs of pathosis prior to treatment. The remaining six teeth presented with pain and widened periodontal ligament spaces. In the first group, twenty nine (93.5%) of teeth healed and in the second group, four out of six (66.6%) teeth healed (Mejare & Cvek 1993). The authors concluded that there was a high frequency of healing in young pulps, provided all carious dentine and the superficial layers of the pulp were removed and the wound dressed with calcium hydroxide.

Pulp Therapy for the Primary Tooth
The vital pulp treatment modalities commonly used in primary teeth are pulp capping (direct and indirect), pulpotomy and partial pulpectomy.

Direct pulp capping is considered only when there is inadvertent exposure of a healthy pulp during cavity preparation. For optimum success, the tooth should be asymptomatic and the exposure site must be pinpoint and free of oral contaminants. Calcium hydroxide is still considered the material of choice for capping (Levine et al. 1988, Fuks 2002). More recently MTA has been successfully employed as a direct pulp capping agent in primary teeth (Bodem et al. 2004, Caicedo et al. 2006). Direct pulp capping should not be considered for cariously exposed pulps in primary teeth. Failure of treatment may result in internal resorption or acute alveolar abscess.

Dentine-bonding agents have also been used for direct pulp capping. In a clinical study, sixty four carious exposed teeth were capped with a bonding agent. After one year, 94% of the teeth were vital (Kashiwada & Takagi 1991).

The rationale for the pulpotomy procedure is based on the ability of the radicular pulp to heal after surgical amputation of the infected coronal pulp (Fuks & Eidelman 1991). The most commonly used dressing material after pulpotomy is formocresol. Paediatric dentists worldwide used a one-fifth dilution of formocresol for vital primary teeth (Avram & Pulver 1989). Several studies have reported good success-rates with formocresol (Fuks & Bimstein 1981, Fuks et al. 1983). Diluted formocresol is equally effective but is potentially less toxic (Fuks 2000).

The safety and efficacy of formocresol is increasingly being questioned. It has been reported that subsequent to formocresol application, the remaining pulp tissue becomes partially or totally necrotic (Langeland et al. 1976). Most authorities recognise that formocresol is potentially immunogenic and mutagenic and are continually trying to find a suitable substitute.

Some studies have shown promising results with ferric sulphate, a haemostatic agent (Fuks et al. 1997, Casas et al. 2004). Other haemostatic techniques such as electrosurgery and laser therapy have also been tried (Udin 1991). A histological study comparing electrosurgery and formocresol pulpotomies showed the results of both techniques to be comparable (Ruemping et al. 1983). In contrast, another study showed that electrosurgical technique caused pathological root resorption and damage in the furcation
region, probably due to excessive heat generation (Shulman et al. 1987).

**Future Directions in Vital Pulp Therapy**

Vital pulp therapy is not always predictable. A new approach to restore tooth structure is biologically based: regenerative endodontic procedures by application of tissue engineering.

Tissue engineering is the science of design and manufacture of new tissues to replace lost parts because of diseases like cancer and trauma. Three key ingredients for tissue engineering are signals for morphogenesis, stem cells and the scaffold of extracellular matrix. Adult stem cells exist as undifferentiated cells until they are exposed to appropriate signals. They can self-replicate for prolonged periods and maintain their multiple differentiation potential throughout the life of the organism. The stem/progenitor cells, present in pulp, differentiate into odontoblasts in response to bone morphogenetic proteins (BMP’s). There are two ways to regenerate dentine, namely, to apply BMP’s or BMP genes directly to the exposed or amputated pulp, or isolate the progenitor cells from pulp tissue, expose them to BMP’s or BMP genes to stimulate their differentiation into odontoblasts and transplant them back (Nakashima & Akamine 2005).

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Vital Pulp Therapy


The Role of Viruses in Periapical Disease

Artika Patel

Introduction

The aim of root canal therapy is to prevent or eliminate apical periodontitis. This is done by eliminating microorganisms from the root canal system by means of chemomechanical debridement of the root canal system. This is followed by obturation of the root canals with the placement of a good coronal restoration to prevent re-contamination. Studies have reported the success of orthograde endodontic therapy to range between 53 to 98% (Sjögren et al. 1990; Ørstavik 1996; Sundqvist et al. 1998). Failures in root canal treatment are commonly seen when treatment procedures do not meet a satisfactory standard for control and elimination of bacteria.

These shortcomings include poor aseptic control, poor access cavity, inability to locate all canals, inadequate instrumentation and poorly sealed restorations (Sundqvist & Figdor 1998). However, failures (seen as persistent infections) are encountered even in cases consistent with the highest standard of treatment (Nair et al. 1999). These failures are not always detected on radiographs due to the limitations of radiographs as a diagnostic tool. Seltzer and Bender have shown that if the cortical bone is intact, a radiograph will not reveal a periapical radiolucency, even with cavitation between the cortical layers (Seltzer & Bender 1961).

The causes for persistent periapical lesion are:
1. Intraradicular infections – a scanning electron microscopy and light microscopy study demonstrated that the major cause of root canal treatment failure is microorganisms in the apical part of the root canal (Nair et al. 1990a).
2. Extraradicular infections – bacteria, infected dentine or cementum chips can become established in the periapical tissue. The bacteria most commonly involved are Actinomyces israelii and Propionibacterium propionicum presenting as periapical actinomycosis (Holland et al. 1980; Nair & Schroeder 1984; Sjögren et al. 1988).
3. Extruded root-canal filling or other material – in the absence of microbial factors, root filling materials which contain irritating substances, can evoke a foreign body reaction in the periapical tissues. This leads to the development of asymptomatic periapical lesions that may remain refractory to endodontic therapy for long periods of time (Nair et al. 1990b).
4. True cysts – the presence of a true cyst can adversely affect the healing process following root canal therapy, resulting in a refractory lesion (Nair et al. 1996).

The role of viruses in periapical pathology and the successful outcome of root canal treatment is often overlooked. Several studies have suggested that viruses have a role in the development of periapical inflammation (Gregory et al. 1975; Simon 1998; Heling et al. 2001; Sabeti et al. 2003a). Rauch (1958) was one of the pioneers of this theory following his chair-side observations. He observed that treatment undertaken in sterile conditions did not show signs of complete healing and teeth often hurt days prior to the onset of viral infections such as colds, influenza or viral pneumonia. Following resolution of the viral infection, he noted that pain in the oral cavity may cease abruptly. Rauch hypothesised that a heterologous antigen besides bacteria prevented complete healing of otherwise sterile areas. He attempted to culture viruses from infected root canals and periapical tissues using monkey kidney cell cultures. No pathogenic viruses were uncovered from the ten cases sampled.

It is well known that the oral cavity is an ecological niche to a diverse microflora consisting of a wide range of viral, bacterial, yeast and even protozoal species (Marsh & Martin 1992). While the role of bacteria in pulp and periapical disease has been well established, the role of viruses in periapical disease has only been investigated in the last two
to three decades. This review paper aims at reporting on the available literature on the role of viruses in periapical disease.

Virus Size, Structure and Replication
It can be said that the virus is the smallest life form (Sällberg 2006). This statement is often disputed, as viruses lack the cellular machinery for self-reproduction and thus the ability to replicate in the absence of a host cell. The Latin term “virus” means poison and this, to some degree, reflects the behaviour of viruses. For example, viruses can be transmitted through the air as small droplets or in some circumstances by the mere touch of the skin by an infected person.

Viruses range from 20-300 nm in size. All viruses have their own genome. The two major groups of viral genome are either RNA or DNA. The genome has two basic functions namely the coding for all viral proteins by the coding region, and interaction with the machinery of the host cells by the non-coding region. A protective coat (termed a capsid or nucleocapsid) encapsulates the genome. This capsid may be either spherical or helical.

Due to their acellular nature, viruses utilize the machinery and the metabolism of the host cell to reproduce. Viral reproduction occurs in various stages. These include:
1. Attachment – binding to the surface of the cell to be infected. This is mediated through an interaction between the surface of the virus and a receptor on the host cell.
2. Injection – depending on the structure of the virus, three mechanisms are used to enter the host cell. If the virus has a lipid membrane, the lipid membrane of the host cell can fuse with that of the virus allowing the viral genome to be released into the cytoplasm. If the virus is a non-enveloped virus (no outer lipid envelope), viral entry into the cell is mediated by either endocytosis or translocation.
3. Replication – once inside the host cell, the virus induces the host cell to synthesize the necessary components to replicate the viral genome.
4. Assembly – the replicated viral components are assembled into new viruses.
5. Lysis – the assembled viruses are released from the cell and the whole replication process begins again (Sällberg 2006).

The detection of viruses in the oral cavity has been a challenge until recently. Previous difficulties were due to the limitations posed by the two main methods of detection namely electron microscopy and tissue culture (Marsh & Martin 1992). Electron microscopy is time consuming and only allows presumptive identification based on morphology. Growth in tissue culture is also laborious and time consuming with the disadvantage that viruses still need to be identified once grown.

The development of specific antisera (a serum that contains antibodies against an antigen of a particular kind) to viruses allow direct identification of viral antigens using radioactive or visual probes. However, this has been largely overshadowed by the polymerase chain reaction (PCR). PCR can amplify even a single target DNA molecule by up to a million-fold. This is matched to a known genome using hybridisation (Leys et al. 2006).

Viruses in Dentistry and Endodontics
Herpes virus
Herpes viruses are large viruses with double stranded DNA genomes. The genome is surrounded by an icosahedral nucleocapsid. The herpes group of viruses include Herpes simplex type 1 and 2 – HSV 1,2, varicella zoster virus – VZV (human herpes virus 3), Epstein-Barr virus – EBV (human herpes virus 4), cytomegalovirus – HCMV (human herpes virus 5) and human herpes viruses 6, 7 and 8 (HHV 6, 7, 8).

The initial herpes virus infection is followed by a latent phase in host cells, ensuring the survival of the viral genome throughout the lifetime of the infected individual. Herpes simplex and varicella zoster establish latency in long-lived non-dividing neuronal cells in sensory ganglia. Cytomegalovirus and herpes virus 6 and 7 establish latency in bone marrow derived myeloid progenitor cells. The Epstein-Barr virus and herpes virus 8 are latent in B lymphocytes (Slots et al. 2003).

Herpes virus transmission occurs by intimate contact with infected secretions including saliva. Herpes virus can be reactivated spontaneously or stimulated by concurrent infection, tissue trauma, drugs, stress or other factors impairing the host immune system. When activated, these viruses activate an array of host responses affecting monocytes, macrophages, T and B lymphocytes, epithelial cells, endothelial cells, fibroblasts and other mammalian cells (Slots et al. 2003).
**Herpes simplex (HSV) 1 and 2**

HSV1 and HSV2 are probably the most common infections in mankind. Around 50% of the population worldwide carries HSV 1 and 5% of population carries HSV 2 (Sällberg 2006). HSV 1 is associated with more than 90% of oral lesions whereas HSV 2 is usually associated with genital infections (Rider et al. 1995).

HSV 1 is mainly transmitted by contact with infected saliva. The most common primary infection is herpetic gingivostomatitis. After the primary infection, HSV 1 travels along axons and lies latent in the sensory nerve cells until reactivated. The migration of the HSV virus through the trigeminal nerve, responsible for innervation of the teeth and alveolar bone, raises the possibility of its involvement in apical pathology.

Rider and associates looked into the evidence of human papilloma virus (HPV), HSV 1 and HSV 2 in a series of radicular cysts (Rider et al. 1995). Radicular cysts and positive control specimens were treated with antibodies directed at each virus. Negative control subjects were not treated with antibodies. All specimens underwent immunostaining. No evidence of HPV, HSV 1 and HSV 2 were found in the radicular cysts. The authors suggested a more sensitive method such as PCR to confirm or refute their findings.

**Varicella zoster virus (VZV)**

VZV also latently infects the sensory neurons and is highly contagious and transmitted through aerosols and direct contact. It causes the childhood disease chicken pox. VZV becomes latent in the dorsal root ganglia or extramedullary cranial nerve ganglia. Reactivation of herpes zoster is termed shingles. “postherpetic neuralgia” and occurs almost exclusively in people over 50 years of age (Solomon et al. 1986). It is thought to be related to waning immune surveillance. This infection is characterised by the appearance of vesicles on the skin along the path of the involved sensory nerve and is associated with severe pain. VZV of the face affects the trigeminal nerve 18.5% of the time (Solomon et al. 1986) and more commonly affects the ophthalmic division (Verbin et al. 1968).

Reported cases of odontalgia associated with varicella zoster involved ruling out other probable causes (Winstock 1966; Nally & Ross 1971). Verbin and associates described a case of severe pain of a right maxillary incisor (pulpitis) as an early sign associated with herpes zoster of the maxillary nerve. The pain remitted spontaneously following healing of the mucocutaneous eruptions (Verbin et al. 1968).

Gregory and associates reported devitalised teeth and facial neuralgia appearing 8 years after an attack of herpes zoster infection (Gregory et al. 1975).

Schwartz and Kvorning (1982) reviewed the literature for post-herpetic complications. These included osteonecrosis of the jaw, tooth exfoliation, periodontitis and scarring of skin. Before exfoliation the teeth were non-responsive to electrical stimulation indicating a possible effect of the virus on the vitality of the pulp.

Solomon and associates (1986) reported root resorption associated with a left, maxillary central incisor and canine four years after an attack of herpes zoster virus while Goon and Jacobsen (1988) reported a unilateral case of 5 devitalised teeth following an attack of shingles.

Several theories exist regarding the role of varicella zoster in the pulp and periapical disease:

- Reactivation of varicella zoster is characterized by 2-3 days of prodromal pain followed by the classic vesicular eruption along the nerve pathway of the involved dermatome. This eruption pattern may include peripheral nerve endings in the pulp leading to pain and possibly pulp necrosis (Gregory et al. 1975, Goon & Jacobsen 1988) or internal resorption (Solomon et al. 1986).

- Intraepithelial vesiculation, oedema and ballooning degeneration can cause elevated intrapulpal pressure. The dental pulp is housed in a non-compliant chamber, allowing little tolerance for increases in intraepithelial...
pressure. Any pressure will thus result in restricted blood flow and ischaemic necrosis. However, the dental pulp is essentially connective tissue and having no epithelial component, cannot undergo “ballooning” degeneration and thus excludes this theory as a possible mechanism (Goon & Jacobsen 1988).

- The theory by Wright and colleagues suggesting that varicella zoster-infected nerve inflames the adjacent vascular tissues resulting in vasculitis and compromised blood flow is more probable. This compromised blood flow eventually causes infarction of the vessels and injury to tissues supplied by the infected nerve endings with pulp death (Wright et al. 1983).

- Smith and colleagues attributed developmental anomalies and root resorption to the disturbance in neurovascular supply following varicella zoster infection (Smith et al. 1984). Garty and colleagues believe that generalised avascular necrosis is unlikely as the maxilla is rich in its vascular supply. They believe the problem is attributed to trigeminal nerve damage compounded by secondary bacterial infection (Garty et al. 1985).

Currently, these theories are based on clinical observation rather than scientific evidence. However, enough case reports have appeared to suggest a connection between herpes zoster infection and pulp vitality and innervation.

**Epstein-Barr virus (EBV) and Cytomegalovirus (HCMV)**

Epstein-Barr virus causes infectious mononucleosis and almost certainly plays a role in the aetiology of nasopharyngeal carcinoma, Burkitt’s lymphoma, and lymphoproliferative disorders in the presence of immunosuppression. The role of Epstein-Barr virus in rheumatoid arthritis, Hodgkin’s disease, and chronic fatigue syndrome is less certain (Slots et al. 2003).

Cytomegalovirus infection is clinically significant in pregnant women, newborn infants with congenital or perinatal infection, immuno-suppressed transplant patients, and individuals with AIDS. Cytomegalovirus is the most common life-threatening infection in transplant and AIDS patients.

HCMV, EBV and other herpes viruses have been implicated in oral ulcers (Syrjanen et al. 1999), aggressive periodontitis and in acute inflammation of the gingiva and oral mucosa (Contreras & Slots 2000). As periodontal disease and periapical infections share similar microorganisms, studies were carried out to determine the role of HCMV and EBV in periapical infections.

Sabeti and associates collected periapical samples from symptomatic teeth for virologic examination. This study employed a cDNA identification analysis to determine transcription of HCMV, EBV and HSV late during the infectious cycle of herpes viruses, thus indicating an active herpes virus infection. HCMV was detected in 12 of the 13 lesions and EBV was detected in 8 of the 13 lesions (Sabeti et al. 2003a). This study provides evidence that HCMV and EBV may play a role in the pathogenesis of symptomatic periapical disease.

A follow up study by the same group confirmed the close relationship between symptomatic periapical lesions and HCMV/EBV infections (Sabeti et al. 2003b).

Periapical lesions harbouring both HCMV and EBV tended to be symptomatic, showed large-scale radiographic bone destruction and harbored higher numbers of anaerobic bacteria (Sabeti & Slots 2004). HCMV was present in all symptomatic periapical lesions, whereas no lesion showed an EBV-mono-infection. Seventy-six percent of symptomatic periapical lesions showed co-infection by HCMV and EBV. Aalto and colleagues hypothesised that HCMV reactivation has the potential to transactivate EBV, thereby resulting in increased pathogenicity (Aalto et al. 1998).

Periapical granulomas contain numerous macrophages, T lymphocytes and B lymphocytes (Marton & Kiss 2000; Metzger 2000). Macrophages and T lymphocytes are host cells to cytomegalovirus, while B lymphocytes are the host cells of Epstein-Barr virus (Slots 2002).

Cytotoxic CD8+ T lymphocytes (Yewdell & Hill 2002) and natural killer cells (Kettering & Torabinejad 1993) are also found in periapical granulomas. Cytotoxic CD8+ T lymphocytes play a major role in the anti-herpes host defence mechanism (Yewdell & Hill 2002). Natural killer cells accumulate at sites of viral replication and
contribute to the host defense mechanism (Biron et al. 1999).

The following is a hypothetical model depicting herpes virus, bacterial and host response in the development of periapical pathosis (Slots et al, 2003):

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“This initially, bacterial infection or mechanical trauma of the pulp causes herpes virus-infected inflammatory cells to enter pulpal tissue through the periapical region. Subsequent herpes virus reactivation gives rise to enhanced inflammatory mediator and cytokine responses in macrophages and other host cells. Lipopolysaccharide from resident Gram-negative bacteria can also stimulate cytokine responses in inflammatory cells. The triggering of proinflammatory cytokines may induce periapical bone resorption or, in a vicious cycle, reactivate latent herpes viral infections. Lowered immune response of the pulp and periapical tissue may lead to overgrowth of pathogenic bacteria or possibly cytotoxicity and tissue necrosis” (Slots et al. 2003).

The herpes virus-bacterial interactions may explain various clinical characteristics of periapical infection. Herpes viruses have periods of latency interrupted by periods of activation. This may be responsible for the “flare-up” of periapical disease. Herpes virus activating factors are also risk factors for acute endodontic disease (Torabinejad 1994). Absence of herpes virus or a lack of endodontic pathogenic bacteria may explain why some teeth with a necrotic pulp can maintain periapical health for extended periods of time.

**Human Immunodeficiency Virus**

Human immunodeficiency virus (HIV) is a retrovirus that can lead to Acquired Immuno-deficiency Syndrome (AIDS) with the potential of developing life-threatening opportunistic infections.

HIV primarily infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages and dendritic cells. HIV infection leads to low levels of CD4+ T cells through three main mechanisms: direct viral killing of infected cells; increased rates of apoptosis in infected cells; and recognition and killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes.

When CD4+ T cell numbers fall below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections. If untreated, most HIV-infected individuals eventually develop AIDS and may die.

**HIV and periapical pathology**

Histological studies of HIV patients have revealed high concentrations of pro-viral DNA present in the pulp tissue. Glick and associates were the first to demonstrate the presence of HIV in the dental pulp of a healthy tooth using PCR (Glick et al. 1989). Due to limitations of the PCR technique at the time, the specific location of the viral DNA in pulp tissue could not be determined.

In 1991, Glick and colleagues demonstrated the presence of HIV in the fibroblasts of non-inflammed dental pulp tissue (Glick et al. 1991) by using PCR and haemotoxylin and eosinophil (H&E)-stained pulp tissues. They claim to be the first to demonstrate and report in vivo infection of the dental pulp fibroblasts by HIV.

It is interesting to note that none of the nerve fibres of the teeth in their study showed evidence of HIV. Neural tissue is one of the principal targets of HIV seen commonly in the deterioration of the neurological function in HIV positive patients. Close to 88% of individuals with HIV have shown HIV infection in their brain tissue at postmortem (Lantos & McLaughlin 1989).

There are only a couple of studies which have investigated the presence of HIV in periapical granulomas of HIV positive patients. Gerner and associates used immunofluorescence staining from a HIV positive patient to assess the presence of HIV in periapical tissue (Gerner et al. 1988). The results showed that T4 lymphocytes were
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extremely rare and that T8 lymphocytes dominated. In AIDS patients the T4/T8 ratio is considerably reduced as T4 lymphocytes are assumed to be the main target cells for HIV. This was reflected in their results.

Elkins and associates (1994) used PCR to assess the presence of HIV DNA in periapical lesions of a HIV positive patient. Their results demonstrated that the periapical lesions from the HIV positive patients contain HIV DNA.

These studies highlight the importance of universal infection control and suggest delayed healing of apical periodontitis due to reduced numbers of T4 lymphocytes following root canal therapy in HIV positive individuals.

Predicting treatment outcome is a potential dilemma when treating immunocompromised patients is. Only a few studies address the possible correlation between a compromised immune system and endodontic treatment outcome. A retrospective study by Fouad & Burleson (2003) showed that in patients with pre-operative periradicular lesions, a history of diabetes was associated with a reduced longterm successful outcome following endodontic therapy.

A more recent retrospective study compared periapical healing between medically healthy patients and HIV positive patients one year after treatment. Even though the healthy patients showed greater radiographic healing the results were not statistically significant (Quesnell et al. 2005).

Conclusion
This review paper reports on the association with, and the role of viruses in the pathogenesis of pulp and periapical disease. Based on the existing evidence, it is recommended that viruses be considered and included as possible aetiological factors during the diagnosis, treatment and healing phases of pulparely and periapically affected teeth.

References


News from The University of Otago

Congratulations to the first group to graduate with Doctorates in Clinical Dentistry (DCID) in Endodontics.

JACK LIN’s thesis was entitled ‘Electric pulp testing of molar teeth’. He is moving to Sydney to establish a specialist practice there.

RAJ ROY’s work was on ‘Theory and practice of resecting and managing root ends’. Raj will be working in New Plymouth when he leaves Dunedin.

DARRYL VIOLICH’s thesis was on ‘Removal and modification of the smear layer: effect on the Prepometer instrument’. Darryl is looking at practicing in the North Island.

DIKESH PARMAR’s work was ‘Detection of dentine tubule infection’. Dikesh is well under way setting up a practice in Wellington.

The four students commenced studies as the first group to do an MDS in endodontics over three years (previous programmes were two years long). They then had the opportunity to ‘upgrade’ to the Doctorate by presenting a thesis rather than a research report. This represented a considerable challenge for both student and supervisors.

Professor Paul Abbott from Perth was the overseas external examiner for all four candidates. Each thesis also had a New Zealand external examiner, and Hani Naoum, Mike Gordon and Scott Turner (two theses) undertook this role. The third examiner for each student was chosen from within the School of Dentistry, with Doug Holborow, Jonathan Leichter, Ann Holmes and Bernadette Drummond involved. Many thanks to all concerned, it was a big effort!

Nick Chandler

Congratulations to Artika Patel who has been awarded a grant by Dentsply to assist with the cost of her clinical doctorate research.

THANK YOU to Dr Andrew Mackie who has recently graduated with his Doctorate in Prosthodontics.

He has kindly donated his Obtura machine to the Department of Oral Rehabilitation.