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Management of deep dentinal carious lesions

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1.Dentin

Dentin a tissue of mesenchymal origin produced by odontoblasts, intimately associated with the pulp, usually termed as dentino-pulpal complexm as shown in Figure (1). Odontoblasts secrete dentin as unmineralized form, then mineralizes through development. The odontoblastic process secretes both collagen and non-collagenous proteins, which including dentin sialophosphoprotein and osteocalcin,these non-collagenous proteins likely serve as the impetus for dentin mineralization.

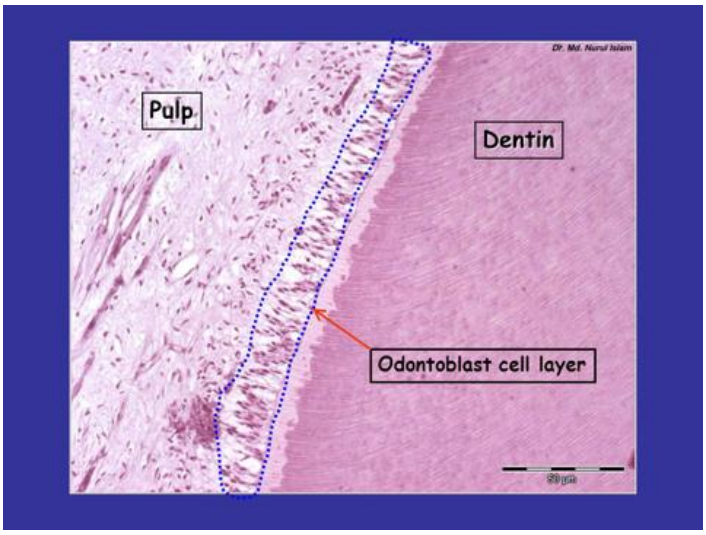

Figure (1) Histological cross section of normal dentino-pulpal complex

Dentin is porous and yellow-hued material. It is made up of 70% inorganic materials (mainly hydroxylapatite and some non-crystalline amorphous calcium phosphate), 20% organic materials (90% of which is collagen type 1 and the remaining 10% ground substance, which includes dentine-specific proteins), and 10% water. it is softer than enamel, so

decays more rapidly and subject to severe cavities if not properly treated, but due to its elastic properties it is a good support for enamel. Its flexibility prevents the brittle enamel fracturing. were noted as tubule numbers increase in proximity to the pulp (Addy M. 2002), so do the number of tubule branches ,as shown in Figure (2).

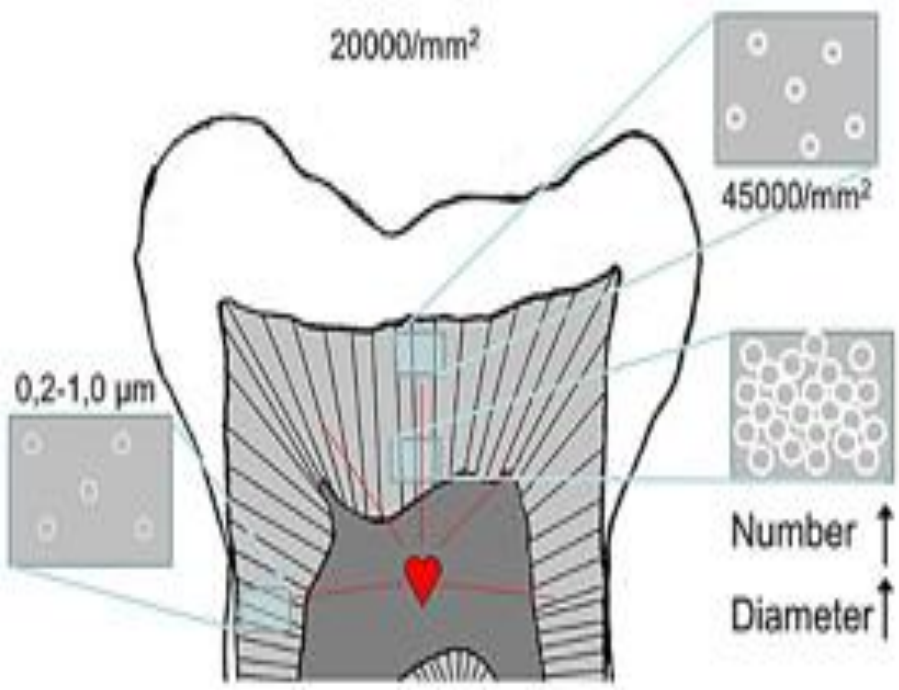

Figure (2) The number and diameter of tubules in relation to the proximity to the pulp

1.1 Classification of dentin according to stage of formation:

Dentin often classified into three basic types, as shown in Figure (3):

1.1.1 Primary dentin :is that which is formed prior to eruption

1.1.2 Secondary dentin: forms after root formation is complete,normally after eruption

1.1.3 Tertiary dentin: develops in response to more intense pulpal irritants like cavities

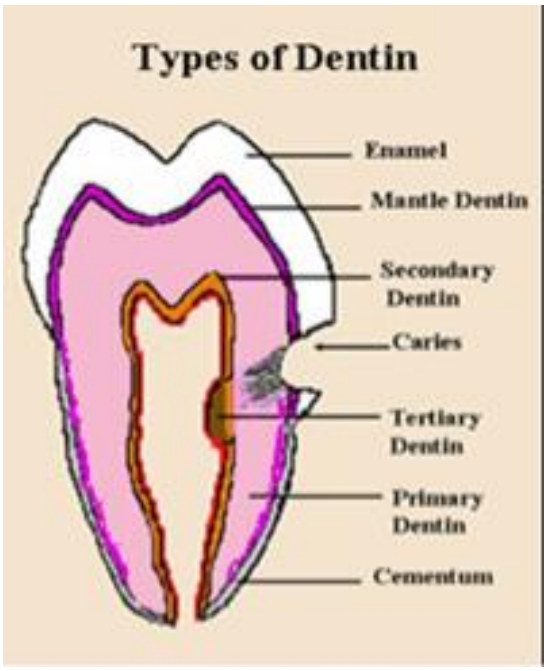

Figure (3) types of dentin according to stage of formation,

There is interface between primary and secondary dentin with a change in tubule direction in addition to the decrease in tubule number

tertiary dentin categorized as reactionary or reparative dentin, Reactionary is formed from an existing odontoblast, whereas reparative dentin is formed by the generation of a new odontoblast from precursor cells (J.H. Kinneya.et al,2005), as shown in Figure (4), An average of (1.49) μm of reparative dentin is formed per day.

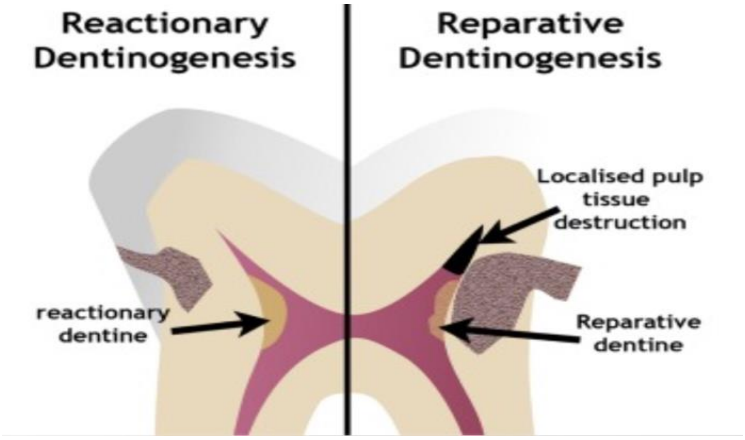

Figure (4) Reactionary and reparative dentin

2. Dental Caries

Dental caries is the name of a disease resulting from the ecologic shift within the dental biofilm by shifting from a balanced population of microorganisms to acidogenic, aciduric, and cariogenic microorganisms' population that developed and maintained by frequent consumption of fermentable carbohydrates. This resulting activity shift in the biofilm is associated with an imbalance between demineralization and remineralization, leading to net mineral loss within dental hard tissues, the sign and symptom is being a carious lesion (Fejerskov et al. 2015).

It is one of the most commonly occurring diseases worldwide and its treatment has high cost implications in monetary and biological (dental pain/infection and tooth loss) terms. Non-operative measures (plaque and diet control and fluoride application) are important treatments to control caries progression. However, operative dentistry (placement of restorations) has a role to play in facilitating plaque control and in restoring tooth form and function. Cavitated lesions that cannot be cleaned are restored to allow the patient to clean effectively.

Histologically & clinically dentinal caries has been characterised as having two distinct layers, as shown in Figure (5):

1- Outer zone where the dentin is highly demineralised, the collagen denatured and heavily infected with bacteria (often referred to as the infected zone or heavily bacterially contaminated zone)

2-Inner zone where the dentin is demineralised but the collagen intact and minimally infected (often referred to as the caries affected zone) (Fusayama 1972).

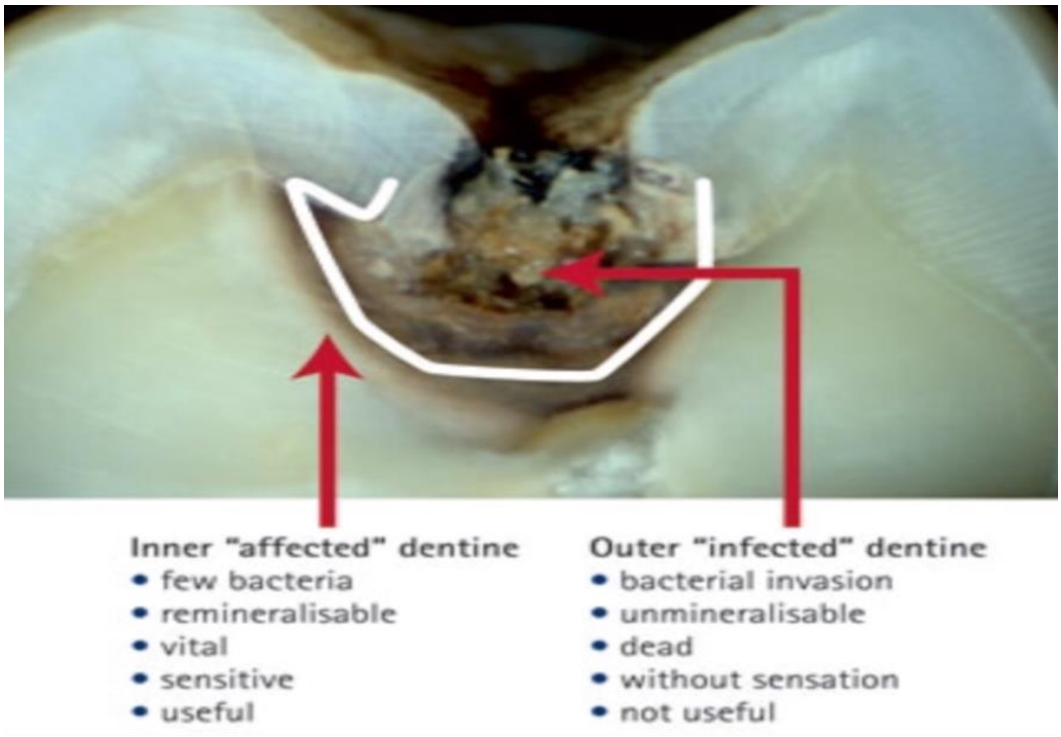

Figure (5) Outer (infected zone) and inner (affected zone) carious dentin.

2.1 Clinical Presentations of carious dentin

Carious dentin can be classified clinically according to tactile sensation by a sharp probe into four categories, as shown in Figure (7):

2.1.1 Soft carious dentin

Soft dentin will deform when a hard instrument is pressed onto it and can be easily scooped up (e.g, with a sharp hand excavator) with little force being required, as shown in figure (6).

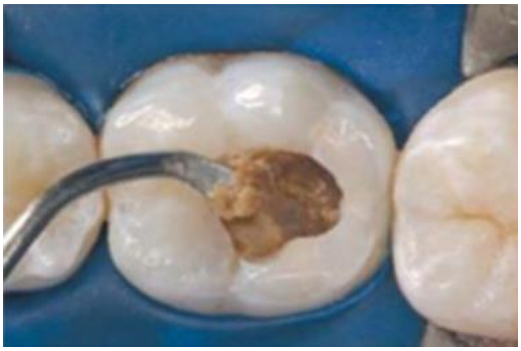

Figure (6) Soft dentin

2.1.2 Leathery Dentin

Although the dentin does not deform when the instrument is pressed onto it, leathery dentin can still be easily lifted without much force being required. There may be little difference between leathery and firm, with leathery being a transition on the spectrum between soft and firm dentin.

2.1.3 Firm Dentin

Firm dentin is physically resistant to an hand excavation, and some pressure needs to be exerted through an instrument to lift it.

2.1.4 Hard Dentin

For hard dentin, a pushing force needs to be used with a hard instrument to engage the dentin, and only a sharp cutting edge or a bur will lift it. scratchy sound or “cri dentinaire” can be heard when a straight probe is taken across the dentin.

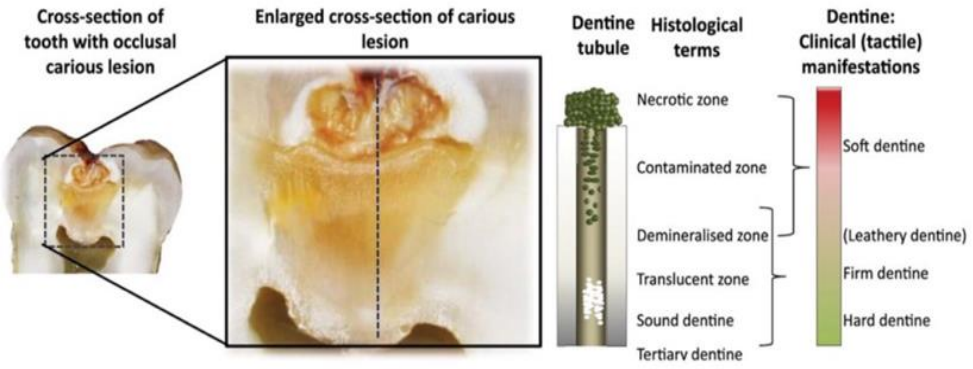

Figure (7) Histological and schematic cross section of a deep carious lesion source: Inness et al, 2016.

3. Pulp damage and repair

Pulp tissue is constantly subjected to environmental impacts. These potential aggressions include (microbial toxins, heat, mechanical trauma, restorative materials, cleaning solutions and cavity liner). Following various injuries, the pulp cells have the intrinsic capacity to repair differentiate into odontoblasts and producing the dentin matrix proteins during wound healing (Chan C .et al ,2005). Even so, not all the inflammatory reaction results in permanent damage.

When the injury is removed before the pulp damage, a repair process begins (Trowbridge H. et al., 2002) and collagen synthesis is accelerated in this phase (Okiji T. and Seltzer et al,2002). The deposition of collagen in the pulp tissue is increased by the action of cytokines. The Collagen synthesis can be improved through the transforming growth factor TGF-β1, TGF-β2 and interleukin (IL)-1β (Barkhordar R. et al ,2002), (Chan C.et al,2005). Fibroblasts at an inflammatory micro environment in which deposit the collagen in a remarkable amount during the inflammatory process as opposed to the normal conditions (Barkhordar R.et al, 2002). The collagen synthesis by fibroblasts during the inflammatory process is a key event for human pulp repair (Chan C.et al, 2005).

Dental pulp stem cells (DPSCs), are mesenchymal-derived cells characterised by self-renewal and multi-lineage differentiation

(including chondrocyte , adipocyte , neural and osteoblast lineage differentiation), establishing them as an attractive choice for tissue engineering and regenerative purposes (Longxing N W.et al ,2015) Numerous studies have demonstrated that DPSCs have the potential to generate dentin and pulp tissues under appropriate environmental conditions (Gronthos S.et al 2000),(Shi S. et al, 2001) In pulpitis, DPSCs can form tertiary dentin adjacent to the injury site by proliferation, migration and differentiation into odontoblast-like cells (Cooper P. et al, 2010).

4. Inflammatory response of the dentino-pulpal complex

Dental caries is a chronic infectious disease, which can lead to the demineralization of enamel and dentin and subsequent pulp tissue injury (Akira S.et al 2006). Pulpitis is an inflammatory disease occur when the infection of caries lesion penetrates the dentinal tubules and into the pulpal tissue (Hahn C. L. et al, 2007). During the inflammatory phase, the pulp tissue reacts to bacterial irritants by innate and/or adaptive immune responses, thus releasing a range of chemokines and proinflammatory cytokines.

Interferon gamma (IFN-γ) is a dimerized soluble cytokine, which is critical for the innate and adaptive immune responses targeted against viral, bacterial and protozoal infections (Schoenborn J. et al, 2007). In contrast with several studies which describe the role of IFN-γ in the immune responses, recent work has now shown that IFN-γ is required for the osteogenic differentiation of mesenchymal stem cells (MSCs) (Gustavo Duque . et al, 2011). Recently, studies have focused increasingly

on the roles of (Interfero-γ) in Dental Pulp Stem Cells , as shown in figure(8).

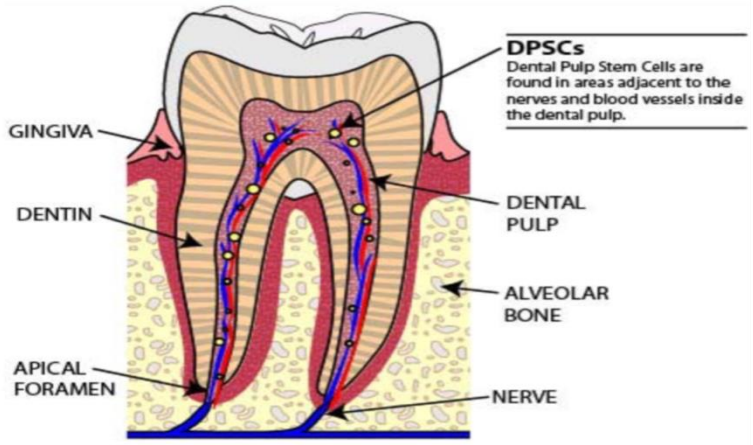

Figure (8): Schematic diagram shows Dental pulp stem cells origin in dental pulp

It has been reported that (IFN-γ) at relative high concentration (100 ng/mL) treatment improved the impaired dentinogenic and immunosuppressive regulatory functions of disease-derived Dental Pulp Stem Cells following pulpitis (Sonoda S. et al, 2016)

Dental caries or trauma can give rise to an inflammatory response in the dental pulp. Gram-negative bacteria (e.g. Fusobacterium, Prevotella, and Porphyromonas) has been reported to be closely associated with,symptomatic teeth , infected pulps and periapical abscesses (Martin F.et al, 2002),(Hoshino E. et al,1985)

Lipopolysaccharides (LPS) is the major component of the membrane of Gram-negative bacteria, has been shown to be responsible for pulp infection and can trigger a protective inflammatory response which is characterised by release of a range of inflammatory cytokines, including

interleukins (IL-1α, IL-1β , and IL-6), TNF-α, and IFN-γ(Ueda M. et al, 2014), Numerous studies have reported that these cytokines can also have significant impact on the behavior of progenitor/stem cells in the pulp, leading to deposition of reparative tertiary dentin in response to the injury.

Nuclear factor kappa B (NF-κB) signaling active in many inflammatory diseases, such as arthritis, gastritis and pulpitis (Monaco C. et al, 2004) studies have demonstrated that NF-κB signaling is involved in regulating odonto/osteogenic differentiation of DPSCs (Minamikawa H. et al, 2009) (Paula-Silva F.et al, 2009).

5. Excavation strategies of deep carious dentinal lesions

5.1 Stepwise carious tissue excavation:

This procedure involve removal of carious tissue on two stages:

Stage 1: Selective removal to soft dentin. Stage 1 has the same carious tissue removal aims as selective removal to soft dentin, with completely demineralized carious tissue, still soft, being left pulpally, but where there is removal of enough carious tooth tissue to place a durable restoration and avoiding pulp exposure. The periphery of the cavity should be hard with similar appearance and tactile characteristics to sound dentin. A provisional restoration is placed with a restorative material that is considered suitable to last up to 12 mo.

Stage 2: Selective removal to firm dentin 6 to 12 month later. The subsequent removal of this provisional restoration should have followed by the stage 2 pathway, selective removal to firm dentin, with placement

of a definitive restoration for longevity. This technique has been known as 2-step excavation (Innes et al.2016).

5.2 Selective carious tissue removal

This procedure involves selectively remove carious tissue to either soft or firm dentin and restore the tooth in single visit without a second stage to remove the remaining carious tissue.

a. Selective removal to soft dentin. Selective removal to soft dentin in deep lesions means leaving soft carious dentin in the pulpal aspect of the cavity. Peripheral enamel and dentin should be hard at the end of excavation to allow the best adhesive seal. This technique has been known as partial carious tissue removal, ultraconservative, or incomplete carious tissue removal. A sharp hand excavator can be used to check the softness / hardness of the remaining dentin; remember that soft dentin will deform when an instrument is pressed onto it and little force would be required to lift (Innes et al,2016).

B-Selective removal to firm dentin. In selective removal to firm dentin, the aim is to excavate to leathery or firm dentin (physically resistant to hand excavator) in the pulpal of the cavity. This is the contemporary understanding of how much should be removed if the entire carious contaminated but not the demineralized dentin, it is acknowledged that are not easily accessible or widely used means to tell when contaminated tissue has been removed and to determine when is seen in the cavity is only demineralized dentin. However, although somewhat subjective, the tactile sense of reaching firm dentin on the pulpal floor, rather than aiming for hard dentin, is probably the best guide that can be given. (Innes et al, 2016).

5.3 No dentinal carious tissue removal

There are various procedures where no dentin carious tissue removal takes place. Although diverse methods are used to carry this out, these procedures effectively serve the same purpose to control the carious lesion without removing any of the diseased dentin tissue from cavity

Resin or glass ionomer sealant materials. Pit and fissure therapeutic sealant materials (resin or high-viscosity glass ionomer cements) can be placed over enamel and dentin carious lesions. However, particularly with unfilled resin, mechanical properties are limited for filling and covering the microcavities in enamel. There are also theoretical concerns about materials' abilities to resist forces occlusally when there is a considerable amount of soft dentin beneath the weakened enamel ("trampoline" effect).in addition, the extent of the lesions where these materials can be used may be limited, pending evidence, to lesions that are confined (on a radiograph) to the outer third of dentin(Innes et al,2016)

The Hall Technique. This is a specific procedure for primary molars where a preformed metal crown (stainless steel) is fitted over the tooth to seal the dentin carious lesions. The crown is cemented with glass ionomer cement over a primary molar tooth and the carious lesion with no tooth preparation or carious lesion removal. It is usually indicated for the approximal lesions. allowing the primary molar to exfoliate without pain infection. Non-restorative cavity control. Other names for techniques that would be encompassed within this strategy include nonoperative caries treatment and prevention (Vermaire et al., 2014) , non-restorative caries treatment (Lo et al. 1998; Gruythuysen 2010 ; Mijan et al. 2014) and slicing preparations. These techniques are broadly similar in that they aim to achieve arrest of a carious lesion using a package of care, through

caries management at a patient level. They aim to prevent further loss of tooth tissue through caries progression in a cleansable cavity by successful instigation of the intensive preventive regimen that included plaque removal (tooth brushing with a fluoridated toothpaste and / or application of fluoride varnish) . From a carious lesion perspective, it may be necessary to alter the shape of the cavity by opening the cavity margins, to allow it to be cleansable, and thus might involve some operative, although not restorative, intervention. These methods tend to be applied to primary teeth but have a role in the permanent dentition, example, in root carious lesions (Innes et al, 2016).

5.4 Complete Removal of Carious Tissues

This term was mean removal until only leathery or firm dentin (resistant to hand excavator) is left pulpally," it was acknowledged that there was still a widely held belief that "removal until only hard dentin is left pulpally .removal of carious lesion to leave only hard dentin throughout the cavity to be over-treatment, involving removal of tooth tissue that did not need to be removed (Thompson et al. 2008; Ricketts et al. 2013; Schwendicke, Meyer-Lückel, et al. 2013). It was also agreed that although the words firm and hard are subjective, they were the best terms.available(Thompson et al. 2008; Ricketts et al. 2013; Schwendicke, Meyer-Lückel, et al. 2013)

Pulpal exposure: At its most extreme, caries removal in dentin lesions can lead to exposure of vital pulp, such exposures in a symptomless tooth have been managed by placement of a direct pulp cap or with a

pulpotomy. These techniques can achieve good success rates when used to treat pulps exposed by dental trauma However, following carious exposures (where infected dentin and pulp is more likely to be compromised) outcomes are poor (Vermaire et al., 2014).

6. Comparison of the clinical outcomes of deep carious tissue excavations' strategies

There are numerous studies assessed the clinical outcome of different strategies of deep carious tissue removal implemented in treatment of deep carious lesions (Bjorndal et al., 2010, Maltz et al., 2012), in terms of pulp exposure, postoperative symptoms and failure of restoration. The recent metanalysis of the randomized controlled clinical trials performed in deep carious lesions using the above-mentioned strategies assessed the risk of pulp exposure and difference in signs and symptoms of the pulp (Ricketts et al., 2013).

6.1 Stepwise excavation versus complete caries removal

There was 56% reduction in risk of exposure of the dental pulp during stepwise excavation compared to complete carious tissue removal. Also, there was no evidence of a difference in signs or symptoms of pulpal disease when comparing stepwise excavation to complete caries removal.

The studies demonstrate that partial caries removal and sealing into the tooth (first stage stepwise) leads to the systematic and progressive arrest of the carious lesion. This allows time for pulp dentin complex reactions, reducing the risk of pulpal exposure when cavities are re-entered at the second visit of stepwise to remove the remaining

demineralised tissue. when the first stage of stepwise excavation caries removal was carried out there was only (1.3%) exposures of the dental pulp compared to (14.3%) exposures at second stage of stepwise (Ricketts et al., 2013).

6.2 Partial caries removal versus complete caries removal

Comparison 2 included three trials (Lula 2009; Orhan 2010 and Ribeiro 1999) which compared partial caries removal to complete caries removal.

-Partial caries removal resulted in a 77% reduction in the risk of exposure of the dental pulp during carious tissue removal compared to complete carious tissue removal. However, there was no significant evidence of reduction in signs and symptoms of the pulp between the two techniques (Ricketts et al., 2013).

6.3 No dentinal caries removal versus complete caries removal

Comparison 3 included two studies (Innes 2007; Mertz-Fairhurst 1986) which compared no dentinal caries removal with complete caries removal. Exposure of the dental pulp during caries removal was not possible in the intervention groups where no dentinal caries removal was carried out. However, it is interesting to note that no exposures of the dental pulp occurred in the control groups of these studies either. This result might be expected in the study as the included teeth had caries radiographically confined to the outer half of dentin. However, in the Innes 2007 study, almost half (42%) of the included teeth demonstrated caries radiographically into the inner half of dentin and some exposures would therefore have been expected in the control group. There are at

least two possible explanations for this lack of pulp exposures during caries removal.

1- the participating dentists may have modified their management due to their very involvement in a clinical trial, the so called ’Hawthorne effect’ (Fernald 2012).

2- although these dentists were assumed to be representative of general practitioners, they volunteered to take part in this trial of a highly conservative approach to caries removal and may have had a general tendency to avoid radical caries removal where there was a risk of exposing the dental pulp.

Innes 2007 reported 3% restoration failure rate in the intervention group, whereas the control group reached 37%. However, the restorations placed in the control group in this study of primary teeth were mainly multi-surface glass ionomer restorations, which have been shown to have poor survival clinically (Chadwick 2007). This failure rate in the control arm was much higher than has been reported from secondary care/specialist practice studies of complete caries removal and restoration (Ricketts et al., 2013).

7. Guidelines during carious tissue removal

1-Preserve non-demineralized and remineralizable tissue

2-Achieve an adequate seal by placing the peripheral restoration onto sound dentin and/or enamel, thus controlling the lesion and inactivating remaining bacteria.

3-Avoid discomfort/pain and dental anxiety, as both significantly influence treatment/care planning and outcomes (methods that are less likely to lead to dental anxiety are preferable).

4-Maintain pulpal health by preserving residual dentin (avoiding unnecessary pulpal irritation/insult) and preventing pulp exposure (i.e., leave soft dentin in proximity to the pulp if required).

5-Maximize longevity of the restoration by removing enough soft dentin to place a durable restoration of sufficient bulk and resilience.

Avoiding pulpal exposure has great impact on the lifetime prognosis of the tooth and long-term treatment costs (Whitworth et al. 2005; Bjørndal et al. 2010; Schwendicke, Stolpe, et al. 2013).

8-Indirect Pulp Protection

In deep lesions, partial caries removal may reduce the risk of further pulp pathology, which can arise from exposure during complete caries removal, particularly in asymptomatic teeth. However, indirect pulp capping should be contemplated only if there are no clinical signs or symptoms of irreversible pulpitis. In a deep dentinal lesion, there is already a high likelihood of pulp involvement from the carious challenge, but it is the level of carious activity that is probably the greatest determinant of successful outcomes for indirect pulp capping. In slower progressing lesions or those in which caries has been either arrested or reduced in activity, a better prognosis is likely. The use of a stepwise technique for excavation of caries, in which caries is removed in increments over several visits rather than in one visit, reduces the risk of accidental mechanical exposure of the pulp and also may slow or arrest lesion development, leading to an improved prognosis for pulp vitality. (Demarco F.et al., 2001)

9.Material used in indirect pulp capping

9.1 Calcium hydroxide

Calcium Hydroxide (CH) solutions have been largely used with increased frequency in the treatment of teeth with deep carious lesions in direct/indirect pulp capping, as shown in Figure (9), because of:

1- their property of stimulating sclerotic reparative dentin formation

2-protecting the pulp against thermal stimuli

3-antibacterial action (Foreman P.et al, 1990), (Stanley H.et al, 1997)

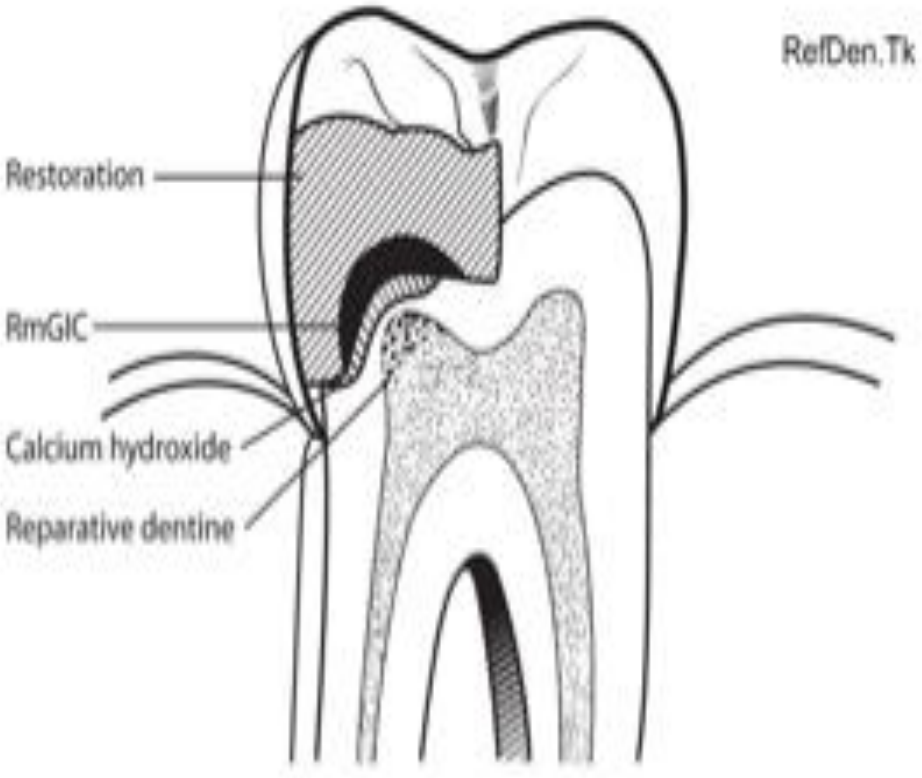

Figure (9) Scheme of the clinical application of Calcium hydroxide in indirect pulp capping.

The first formulation of CH was introduced in dentistry by Hermann (1920) and presented the capacity to induce pulp tissue to form a mineralized barrier, blocking the exposed surface.

CH is a multipurpose agent and there are several indications for its clinical application. Some of its indications include

1- direct and indirect pulp capping

2-apexogenesis

3-apexification

4-treatment of root resorption, iatrogenic root perforations, root fractures, replanted teeth and interappointment intracanal dressing (Farhad A.et al., 2005).

CH is certainly one of the most studied dental materials and it is classically used as the gold standard in biocompatibility tests due to its direct or indirect effect on exposed pulp repair. It is the material of choice for all pulp conservative treatment because of its biological and therapeutic potential (Demarco F.et al., 2001)

CH, in dry powder, suspension or cement form, many studies indicate pulp repair and hard tissue barrier formation when exposed pulp tissue is directly capped with different CH formulations, as shown in Figure (10).

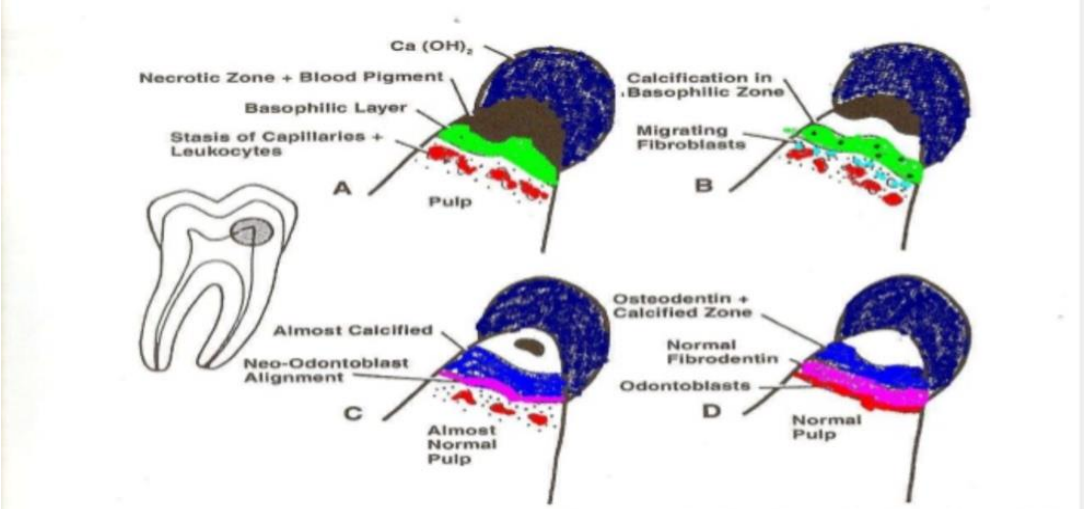

Figure 17-7 Effect of calcium hydroxide and time on the healing of the capped pulp. A, Twenty-four hours after application hydroxide. B, After 2 or 3 weeks. C, After 4 or 5 weeks. D, After 8 weeks. Reproduced with permission from Vermeersch AG.[107]

Figure (10) Mechanism of hard tissue formation after calcium hydroxide application.

It provides a natural protection against the infiltration of bacteria and chemical products (Holland R.et al,1 979). However, the importance of calcified hard tissue barrier formation after capping has been challenged by other studies, which have shown multiple tunnel defects and cell inclusions in bridges following pulp capping with CH. This may lead to leakage and bacteria penetration into pulp tissue unlike the permanent seal produced by bonding agents (Goldberg F.et al, 1984) (Pereira JC.et al, 2000). These tunnels not caused by the CH itself is but are

1- a consequence of the severity of the trauma to the pulp
2- the number of vessels injured during the mechanical exposure.

It has been observed that inside the tunnels there are blood vessels, which maintain the calcium source to the necrotic tissue. The calcium ions in the necrotic layer are responsible for partial dystrophic calcification of the coagulation necrosis. Another type of defect in hard tissue barriers, when present, is represented by cellular inclusions

generally situated between the coagulation necrosis and the calcification zone(Pereira J.et al, 2000) The presence of a hard tissue barrier must be recognized not only as a structural barrier against future injuries, but also as a sign of biological recovery, represented by odontoblast activity (Stanley H.et al., 1997). Yoshiba, et al. (1996) reported findings that support the hypothesis that the differentiation of pulp cells into odontoblasts during reparative dentinogenisis is mediated by fibronectin, which is associated with the initially formed calcified layer after pulp capping with CH (Yoshiba K.et al, 1996)

Classical microscopic studies have shown that CH produces a superficial pulp necrosis and forms calcium carbonate, whose globules act, in a first moment, as dystrophic calcification nucleus, in the margin and in the interior of the dense reticular fiber deposition, immediately beneath the granular zone, where odontoblast-like cells differentiate and organize to produce dentin. The cauterization effect of CH is essential for the repair of exposed pulp (Pereira J.et al., 1980)

It has been suggested that the pH increases due to the presence of free hydroxyl ions may initiate mineralization (Tronstad L.et al, 1981) although other alkaline compounds, such as barium hydroxide and calcium phosphate, failed in this process (Mitchell O .et al 1958). The alkaline pH can neutralize the lactic acid secreted by osteoclasts and may help preventing mineral tissue destruction. CH can act as a local buffer against the acid reactions produced by the inflammatory process (Heithersay GS,1975) suggested that the calcium ions can reduce capillary permeability, thus low intercellular fluid produces increasing calcium ions concentration at the mineralization area (Heithersay G,1975).

In spite of all these advantage CH have disadvantages; CH is soluble in water and acid and its physical properties are deficient (Stanley HR.et al, 1997).The multiple tunnel defects present a morphological disruption of the dentin bridge barrier, in that they fail to provide not only a solid barrier, but also a long-term biological seal against bacterial infection so permit oral contaminants, such as bacteria and their toxic factors, to eventually gain access to the pulp tissue through the marginal gap formed at tooth/restoration interface (Stanley HR.et al,1997) this leakage is responsible for pulp inflammation and necrosis (Stanley HR.et al, 1997).

9.2 Mineral trioxide aggregate (MTA)

MTA is a mixture of a refined Portland cement and bismuth oxide, and are reported to contain trace amounts of SiO_2, CaO, MgO, K_2SO_4, and Na_2SO_4 (Dammaschke T.et al, 2005). Although it may be inferred that Portland cement could serve as a MTA substitute, it is important to emphasize Portland cement and MTA are not identical materials (Robertsa HW.et al, 2008). Few reports exist on the clinical applicability of Portland cement (Conti TR.et al, 2009) (Sakai VT.et al, 2009)

MTA products have been reported to have a smaller mean particle size, contain fewer toxic heavy metals, has a longer working time, and undergo additional processing/purification than regular Portland cements (Islam I.et al 2006).

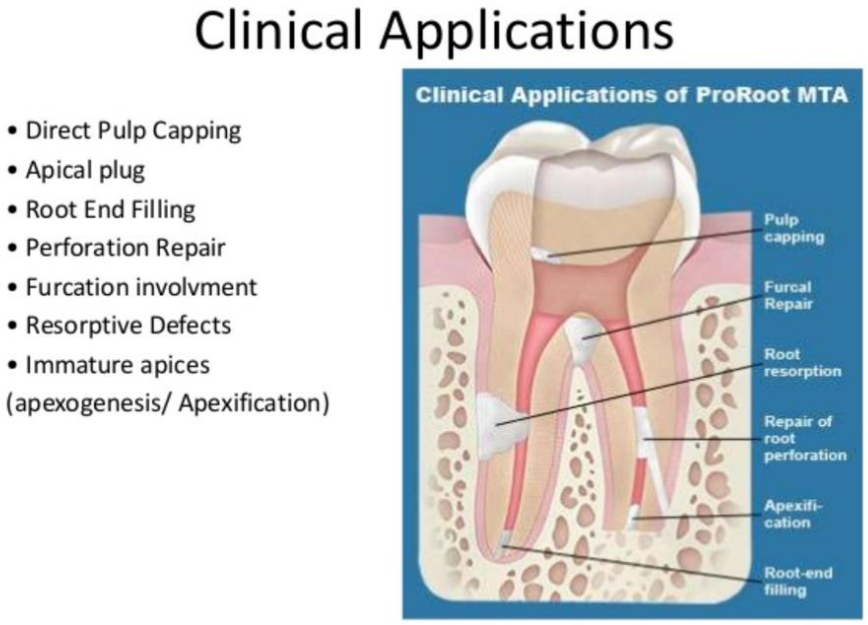

Figure (11) Clinical applications of MTA.

The clinical effectiveness of MTA attributed to the formation of calcium hydroxide when MTA interact with water, However, calcium release from MTA materials diminishes slightly over time (Duarte MA.et al, 2003).MTA materials were reported to form a porous matrix characterized by internal capillaries and water channels in which increased liquid/powder mixing ratio produced more porosity and increased solubility (Fridland M.et al 2003). Grey MTA solubility levels have been reported to be stable over time, but the usually reported pH between 11 or 12 may slightly decrease (Fridland M.et al, 2005) The high pH level of MTA materials has led some authors to theorize that the biologic activity and its biocompatibility is due to the formation of CH (Duarte MA.et al, 2003, Fridland M.et al, 2003, Fridland M.et al 2005). Both White MTA and Grey MTA have been shown to possess antibacterial and antifungal activities, which are presumably due to its pH.

The cytotoxicity of GMTA, amalgam and ZOE was measured using a cell viability assay for mitochondrial dehydrogenase activity in human periodontal ligament fibroblasts after 24 h of exposure to extracts of varying concentrations of the tested materials, in both freshly mixed and 24-h set states (Keiser K.et al, 2000).

A prospective study compared CH and GMTA as permanent dentition pulp-capping medicaments and concluded that CH specimens were hallmarked by tissue inflammation with a 0.15-mm thick dentinal bridge with adjacent pulp tissue necrosis noted at 6 months (Aeinehchi M.et al, 2002). These findings were in contrast with those for GMTA specimens displaying mild tissue reactions with a 0.28-mm and 0.43mm dentin bridge noted at 2 and 6 months, respectively, as well as absence of pulp tissue inflammation, associated with a near-regular odontoblastic layer (Aeinehchi M.et al, 2002).

9.3 Adhesive systems and resin composite

Although physical properties of resin composites are being improved constantly, in vivo studies have shown that the use of resins as restorative materials is occasionally associated with irritation and necrosis of the pulp (Baume LJ.et al 1968), (Stanley HR.et al 1975)(Stanley HR.et al 1967) and periodontal tissues (Nasjleti CE.et al,1983).

Most components of the adhesive systems and resin composites, such as bisphenol A-glycidyl methacrylate (Bis-GMA), urethane dimethacrylate (UDMA), triethylene glycol dimethacrylate (TEG-DMA), camphoroquinone, 2-hydroxyethyl methacrylate (HEMA) and others, have been shown to have definite cytotoxicity when in direct contact with mammalian fibroblasts (Hanks CT.et al, 1991), the most cytotoxic monomers were Bis-GMA and UDMA, which caused irreversible effects

on the cellular metabolism (Hanks CT.et al, 1991). These monomers, when applied on dentin discs, even in the presence of internal pressure, are able to diffuse through the dentinal tubules and reach the pulpal space in concentrations directly proportional to the molecular weight of the monomeric materials (Bouillaguet S.et al, 1996). Resin composite components can be leachable when the degree of conversion is not reached (Ferracane JL.et al ,1991) or when the resin is degraded by esterase from saliva or when hydrolytic degradation occurs (Freund M.et al,1990).

Adhesive resin systems are used to enhance retention, reduce microleakage, and decrease postoperative sensitivity of composite resin restorations. In vivo studies have demonstrated that the application of an adhesive resin directly onto a site of pulp exposure, or to a thin layer of dentin (less than 0.5 mm), causes dilatation and congestion of blood vessels as well as chronic inflammatory pulpal response. Complete polymerization of adhesive resins might be unachievable during direct pulp-capping procedures due to the presence of the pulpal edema. In addition, it has been shown that the oxygen prevents complete polymerization of adhesive resin monomers (Gerzina TM.et al 1996). Consequently, unpolymerized monomers released from the resin-based material can diffuse directly into the pulp at the exposure site, as well as diffuse through the dentinal tubules to cause cytotoxic effects to the pulp cells (Pashley DH. 1988).

Only a few studies with human teeth have been performed to indicate whether or not dental materials can be used for pulp capping of dental cavities with or without pulp exposure. An adhesive system and a CH paste were placed directly on exposed pulps (Hebling J.et al, 1999) and after seven days, a large area of neutrophil infiltrate underlying the

adhesive system and death of adjacent odontoblasts were observed. The neutrophil reaction was replaced by fibroblast proliferation with macrophages and giant cells surrounding globules of resin scattered in the coronal pulp tissue. The persistent inflammatory reaction and hyaline alteration of extracellular matrix inhibited complete pulp repair or dentin bridging. In contrast, at the 7th day, the pulp tissue capped with CH exhibited odontoblast-like cells organized underneath a zone of coagulation necrosis, pulp repair and apparent complete dentin bridge formation after 60 days. These findings suggested that adhesive systems seem to be indicated for direct pulp capping of human teeth (Hebling J.et al 1999).

9.4 Glass Ionomer cement (GIC)

GIC were developed by Wilson and Kent, in 1971, and introduced in the market in the early 1970s. Their popularity is due to the fact that these materials present several important properties (Ogura N.et al, 2005) such as:

1-fluoride release

2-coefficient of thermal expansion and modulus of elasticity similar to dentin

3-bonding to both enamel and dentin, that’s why they have been used in Sandwich technique with resin composite in enamel deficient areas, as shown in Figure (12):

4-biocompatibility

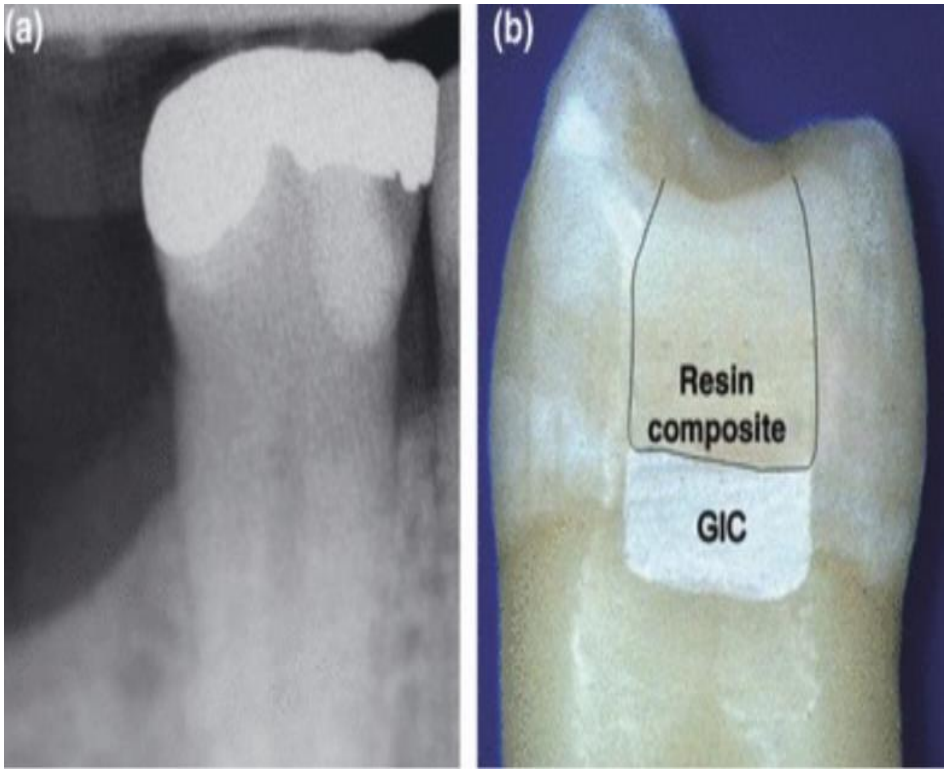

Figure (12) GIC use in Sandwich technique with resin composite in areas with no enamel

Despite these advantages, conventional GICs possess limitations as restorative materials, which are related to their susceptibility to dehydration and poor physical properties, such as high solubility and slow setting rate (Mount GJ, 1994). Developments in the field of GICs have led to the introduction of light-activated hybrid GIC versions creating the resin-modified GICs (RMGICs) (Sidhu SK.et al 1995).

possible cytotoxicity of some ions that are present in significant amounts in GICs, such as F-, Al3+, Zn2+ and Sr2+. The zinc was the only component that was found to be of a sufficiently high concentration to induce cytotoxicity (Stanislawski L.et al,1999).

9.5 Resin modified glass ionomer cement (RMGIC)

Developments in the field of GICs have led to the introduction of light-activated hybrid GIC versions creating the resin-modified GICs (RMGICs).

The degree of monomer conversion of the RMGICs has not been determined, several studies have demonstrated that measurable quantities of HEMA are released into the storage solutions used (Aranha AMF.et al, 2006). Leached residual HEMA can easily diffuse through the dentinal tubules due to its hydrophilicity and low molecular weight, thus reaching dental pulp cells (Aranha AMF.et al ,2006).

The application of RMGICs directly onto dental pulp cells is not recommended (Lan WH.et al 2003). However, current in vivo studies performed in human teeth have demonstrated that the RMGIC Vitrebond (3M/ESPE) applied as a liner in very deep class V cavities caused no inflammatory pulp response (Costa CA.et al, 2003)(Costa CAS.et al 2007)In this way, it seems that the presence of a dentin barrier between this kind of light-cured RMGIC and the pulp cells may prevent pulpal damage.

The magnitude of the damage that may be caused by residual monomers to the pulp cells is inversely proportional to the remaining dentin thickness between the cavity floor and the pulp tissue (AranhanA MF .et al 2006)

The toxicity was due to the presence of unpolymerized monomers, such as HEMA and TEGDMA, and polyacrilic acid, which were leached from resin modified materials and metal-reinforced GIC, RMGICs have been shown to be more cytotoxic than conventional GICs (Aranha AMF.et al, 2006) although they may not be as biocompatible as conventional GICs (Stanislawski L.et al 1999).

9.6 Biodentine

a bioactive tricalcium silicate (Biodentine, Septodont, France) was introduced for use in vital pulp therapy for

1-direct pulp capping

2-pulpotomy

3-indirect pulp capping.

4-perforations

5-internal and external root resorption

6-apical surgery, as shown in Figure (13):.

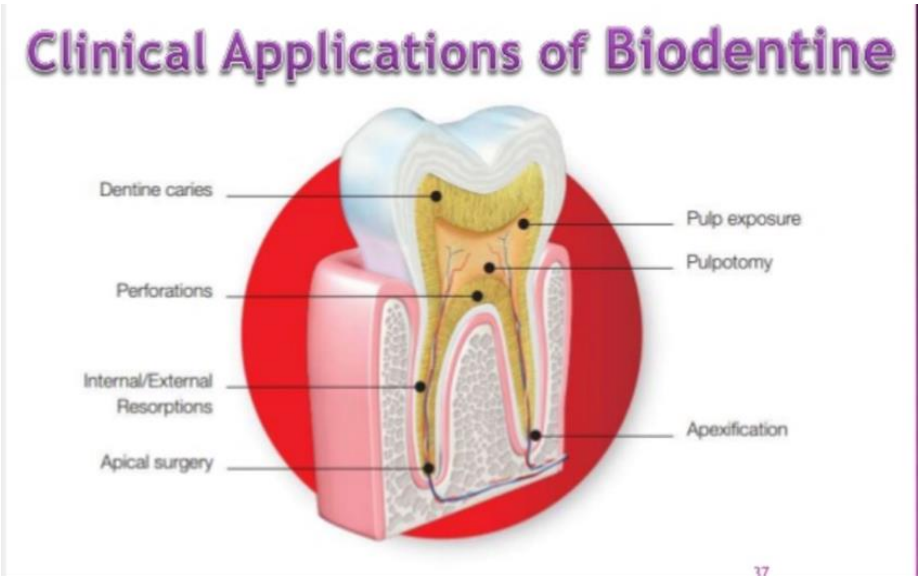

Figure (13) Clinical applications of Biodentine.

Recent studies evaluating a medical grade calcium silicate-based material (Biodentine, Septodont) and techniques for vital pulp therapy have been very positive. As part of the chemical setting reaction of Biodentine calcium hydroxide is formed. Biodentine has demonstrated bioactivity and formation of apatite (Goldberg M. et al 2009), Other research has described the ability of the tricalcium silicate-based cement to induce reparative dentin synthesis by modulating pulp cells to secrete TGF-ß1 and stimulate dental pulp mineralization Bioactive tricalcium

silicate has several advantages over calcium hydroxide and mineral trioxide aggregates (MTA). The commercialized tricalcium silicate is different from the usual dental calcium silicate “Portland Cement” materials. The manufacturing process of the active biosilicate technology eliminates the metal impurities seen in the “Portland Cement” calcium silicates. The setting reaction is a hydration of tricalcium silicate which produces a calcium silicate gel and a calcium hydroxide. In contact with phosphate ions, it creates precipitates that resemble hydroxyapatite (Colon P.et al 2010), these precipitates from MTA and tricalcium silicate can be incorporated into root canal dentin (Han L.et al 2011).

Histologically, the bioactive tricalcium silicate demonstrated the ability to induce odontoblast differentiation from pulp progenitor cells. The resulting mineralized matrix had the molecular characteristics of dentinAn evaluation comparing the biocompatibility of the tricalcium silicate with MTA and Dycal demonstrated that the Biodentine was equivalent to MTAand more biocompatible than Dycal (Laurent P.et al 2008) A clinical evaluation over 6-35 months of Biodentine as a base and for pulp capping demonstrated both biocompatibility and longevity (Koubi GF.et al 2009).

Furthermore, Biodentine is faster setting than other calcium silicate cements, allowing it to be used as a liner and as a dentin substitute base under definitive restorative materials (Bentley K.et al, 2012). Sluyk and coworkers reported that MTA required a setting time of 72 hours to resist displacement and dislodgement from dentin walls of a preparation (Boksman L.et al 2011), Within 35 minutes from placement MTA demonstrated insignificant setting and within 24 hours it had only 23% of the compressive strength of the material at 28 days (Bentley K.et al 2012). It has been recommended that restoring the tooth, MTA should be

covered with a light cured glass ionomer liner after placement because of MTA's extended setting time (Yapp R.et al 2012).

A study comparing Biodentine to two commercially available liner/base materials, Fuji IX (GC America) and VitreBond (3M-ESPE) in their resistance to compressive deflection when covered with a restorative composite resin, demonstrated that after 10-minute setting time all three tested materials supported the composite resin at a clinically relevant load (Yapp R.et al 2012). Biodentine is faster setting than other calcium silicate cements allowing it to be used as a liner and a dentin substitute base under definitive restorative materials (Horowitz A.et al 2011).

9.7 conclusions

1. In human pulps, direct pulp capping with adhesive systems produces different degrees of pulp inflammation, even without bacterial presence and absence of dentin bridge formation as well as pulp repair. Some studies support the idea that when hermetic seal of cavity is obtained, the dentin-pulp complex protection materials are unnecessary, and they not influence the pulp repair, but hermetic seal of the restoration is difficult to be obtained.

2. RMGICs are more cytotoxic to the pulp cells than conventional GICs due to the presence of unpolymerized monomers and should not be applied directly to the pulp tissue.

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