Introduction:

The present study guide is unique in the sense that it encompasses both classic and most recent literature (2015) in the field of Endodontics. By combining the important studies most commonly repeated in the previously available lit review guides, as well as the recent noteworthy current literature, our goal is to create a comprehensive guide for aspiring endodontists who are preparing to become board certified. Also, heavy emphasis was placed on the clinical relevance of the studies in order to create a resource that would aid endodontists in their endeavor to practice the best evidence-based endodontics. The material used to put this guide together includes Dr. Peter Z. Tawil and Dr. Keith Krell's study guides in addition to all the study materials made available by the College of Diplomates. We acknowledge the work that has been done to put the above-mentioned resources together and hope residents and board candidates would find this guide helpful as they prepare for the process of board certification.

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27	Andreasen JO, Borum MK, Jacobsen HL, Andreasen FM. Replantation of 400 avulsed permanent incisors: 4—factors related to periodontal ligament healing. Endod Dent Traumatol 1995;11:76–89.	175
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How to differentiate Lesion of Endodontic origin and Non-LEOS?!?

LEOS	NON-LEOS
Lamina Dura - Discontinuous	Lamina Dura - Intact
Associated tooth non-vital	Associated tooth always vital
Well Circumscribed lesion	Lesion with indistinct borders
Tear drop shaped/ unilocular	Lesion may be multilocular/ unilocular
Lesion is associated with the tooth on angled radiographs	Lesion changes position with different angled radiographs and can separate from the tooth
Slow growing	Fast growing
Radiolucent	May be radiolucent or radiopaque
Responds to Antibiotics	Not likely to respond to antibiotics
Swellings - associated with pain	Painless swellings possible

Non-leos:
1)Actinomycosis: sulfa granules & multiple sinus tracts
2)Fibro-osseous lesions: PPOF

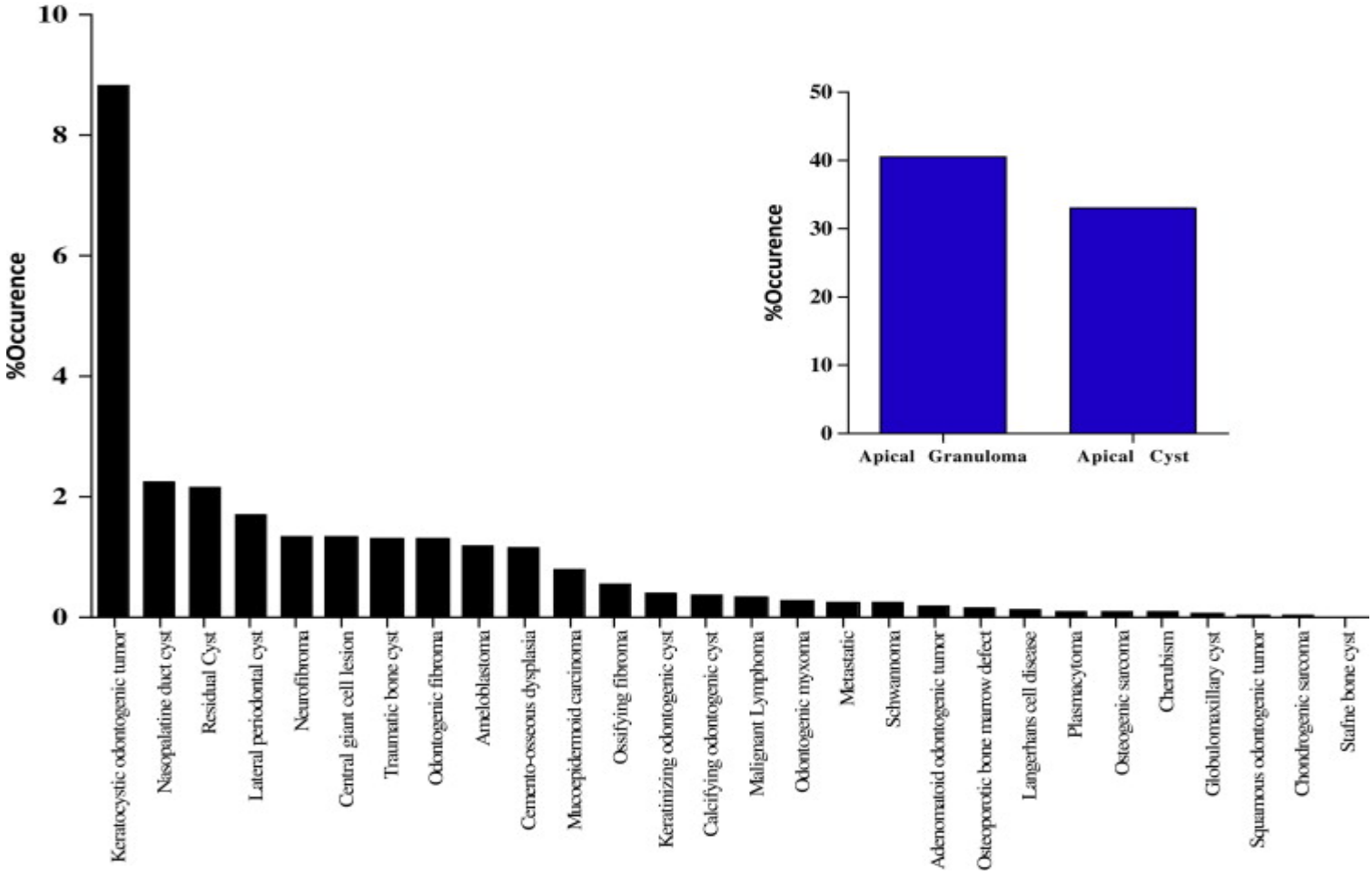
a. Paget's disease
b. Periapical cement-osseous dysplasia
c. Ossifying fibroma
d. Fibrous dysplasia

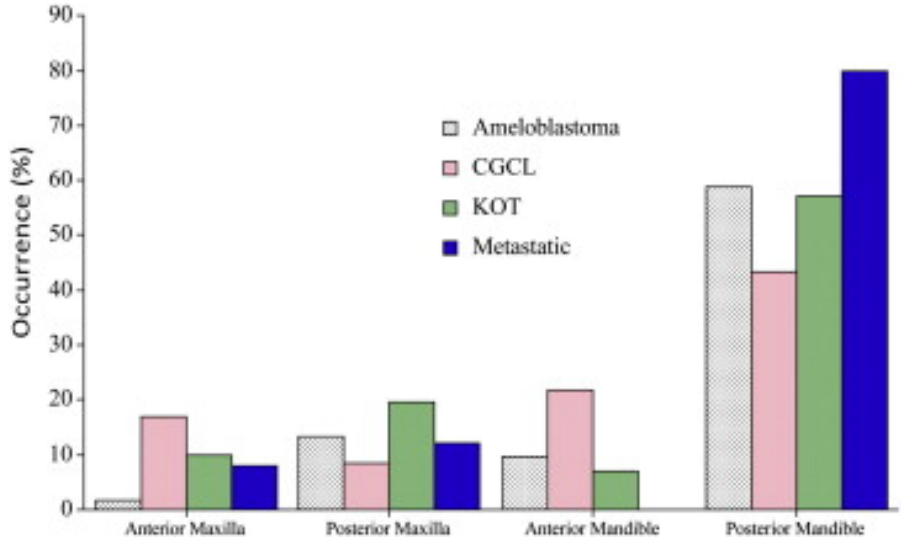
3)OKC (KOT Keratocystic Odontogenic Tumor)
4)Carcinoma
5)Lymphoma (Types of Lymphoma: Hodgkin, Non-Hodgkin and Burkitts Lymphom)
6)Traumatic bone cyst
7)Nasopalatine duct cyst
8)Residual bone cyst
10)Ameloblastoma
11)Central giant cell granuloma
12)Benign cementoblastoma
13)Central odontogenic fibroma
14) Histiocystosis X(Langerhans disease)
15) Leukemia –
16)Osteomyelitis

Non-leos slowly growing - Leos respond to antibiotics - Leos tooth is non vital – not attached to root – well circumscribed –

1. Lamina dura usually intact
2. Ragged borders, fuzzy outline of bone – cancer, etc – not well corticated
3. Lesion moves on PA's (not attached to root)
4. Multilocular
5. Vital tooth
6. Fast growing/expanding
7. Not likely to respond to Ab
8. Radiolucent/radiopaque
9. Paresthesia

Tyler Koivisto (2012, JOE) investigated the location and incidence of all radiolucent jaw lesions in a retrospective study (From Koivisto et al):




Occurrence (%)
90
80
70
60
50
40
30
20
10
0
Ameloblastoma
CGCL
KOT
Metastatic
Anterior Maxilla
Posterior Maxilla
Anterior Mandible
Posterior Mandible

Basics:

Major Subclasses of Immune Cells and Their Major Actions (Courtesy of Ildikó J. Márton 2014 JOE)

Subclasses of immune cells	Major actions	Major released mediators
Antigen presenting cells (APC)	Uptake and processing of antigens and displaying them to T cells	Depending on the subtype of APC (see below)
B cells/lymphocytes	Formation of antigen-specific antibodies; performing as APCs	Fully activated B cells (plasma B cells/plasma cells) secrete antibodies
DCs	Function as professional APCs, innate recognition of microbes by TLR, regulate other immune cells including T and B cells	mDCs produce TNF-α and cytokines of the IL-1 and IL-12 families; pDCs produce type I interferons
LCs	mDCs of the mucosa and skin	Similar to other mDCs
Macrophages (together with monocytes, macrophages are called MNPs)	Develop from monocytes; function as professional phagocytes, and APCs; release toxic compounds that destroy microbes and innocent bystander host cells; regulate immune cells	Cytokines: IFN-β, IFN-γ, IL-1α, IL-1β, IL-6, IL-10, IL-15, IL-18, migration inhibitory factor, TGF-β TNF-α; chemokines: CCL-2CCL-3,CCL-4, CCL-5, CCL-22, IL-8, macrophage inflammatory proteins; reactive oxygen and nitrogen intermediates; eicosanoids; proteases
Mast cells	Anaphylactic type of allergic reactions; nonspecific antimicrobial defense; wound healing; immunoregulation	Histamine, serotonin; eicosanoids; cytokines: IL-1β, IL-3, IL-4, IL-5, IL-13, GM-CSF, SCF; chemokines: CCL-2, CCL-5, exotoxins
MOs	Phagocytosis, antigen presentation, give rise to mDCs and macrophages	Similar to mDCs and macrophages
NK cells	Cytotoxic lymphocytes of innate immunity, contribute to self-tolerance and immune memory	Cytotoxins: perforin, cytotoxins: perforin, chemokines CCL3, CCL4, and CCL5; cytokines IFN-γ, GM-CSF, and TNF-α
NKT cells	CD1d-restricted T cells; recognize lipids and glycolipids; rapid release of soluble regulatory mediators	Cytotoxins as NK cells; IL-2, IL-4, IL-13, IL-17, IL-21, IFN-γ, GM-CSF, TNF-α
PMNs	Of the 3 types of PMNs (basophilic, eosinophilic, and neutrophilic), neutrophils play a major role in apical periodontitis: provide first line of defense against pathogens by phagocytosis; attract and stimulate further PMNs, MOs, and	Reactive oxygen and nitrogen intermediates; proteins with antimicrobial activities: acid hidrolases, defensins, lactoferrin, lysozyme; proteases destroying microbes and host tissues; eicosanoids;

Subclasses of immune cells	Major actions	Major released mediators
	macrophages; destroy periapical tissue components	cytokines and chemokines: IL-1β, TNF-α, IL-8, and CXCL-10
T cells/lymphocytes	Participate in cell-mediated immune reactions as effectors and regulatory cells	Depending on the subtype of T cells
Cytotoxic T cells (CD8-positive T cells)	MHC class I–restricted cells, destruction of infected cells	Cytotoxins: NK cells; cytokines: IFN-γ, IL-2, GM-CSF; TNF-α; chemokines: CCL-3, CCL-4, CCL-5
Memory T cells (CD45RO-positive cells)	Rapid expansion to effector T cells upon antigen re-exposure	IFN-γ, IL-4, IL-17
Helper T cells (Th) (CD4-positive T cells)	MHC class I–restricted cells;promote maturation of B cells, activation of T cells and macrophages; differentiate into several subtypes, which produce stimulatory and inhibitory cytokines	Activated Th cells: IL-2; subset of activated Th cells: IL-17; Th1 cytokines: IFN-γ, TGF-β; Th2 cytokines: IL-4, IL-5, IL-6, IL-10, IL-13; Th17 cytokines: IL-1, IL-6, IL-17, TNF-α
Regulatory T cells (Treg) (CD4+/CD25hi/Foxp3+cells)	Suppress activation of the immune system by secreting regulatory cytokines and by cell-to-cell contacts	TGF-β and IL-10

APCs, antigen-presenting cells; DCs, dendritic cells; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN-β, interferon beta; IFN-γ, interferon gamma; IL, interleukin; LCs, Langehans cells; MDCs, myeloid dendritic cells; MNPs, mononuclear phagocytes; MOs, monocytes; NK, natural killer; NKT, natural killer T; pDCs, plasmacytoid dendritic cells; PMN, polymorphonuclear leukocyte; TLR, Toll-like receptor; TNF-α, tumor necrosis factor alpha

Review of Cytokines involved in pulp-periapical pathogenesis (Courtesy of Elisabetta Cotti JOE, 2014)

Cytokines

Ligands (L)	Cell type	Action	Action on pulp
IL-1α, β	Macrophages, monocytes, lymphocytes, keratinocytes, microglia, megakaryocytes, neutrophils, fibroblasts, synovial lining cells	Pyrogen agent, stimulates differentiation of T_H17 cells, hematopoiesis	Stimulates resorption of the periapical bone but also has a protective role against infection spread; inhibits pulp fibroblasts proliferation; induces expression of collagenase
IL-1Ra	Monocytes, macrophages, fibroblasts, neutrophils, endothelial and epithelial cells, keratinocytes	Antagonist of IL-1	May have a crucial role in the progression of the apical lesions
IL-2	$CD4^+$ and $CD8^+$activated T cells, dendritic cells, NK cells	Proliferation of effector T and B cells, development of Treg cells, differentiation and proliferation of NK cells and growth factor for B cells	Proinflammatory effects; comparable levels of IL-2 have been found in normal, inflamed, and necrotic pulps
IL-4	T_H2 cells, basophils, eosinophils, mast cells, NKT cells, g/d T cells	induction of T_H2 differentiation, IgE class switch, up-regulation of class II MHC expression on	May stabilize the dimensions of the chronic lesions

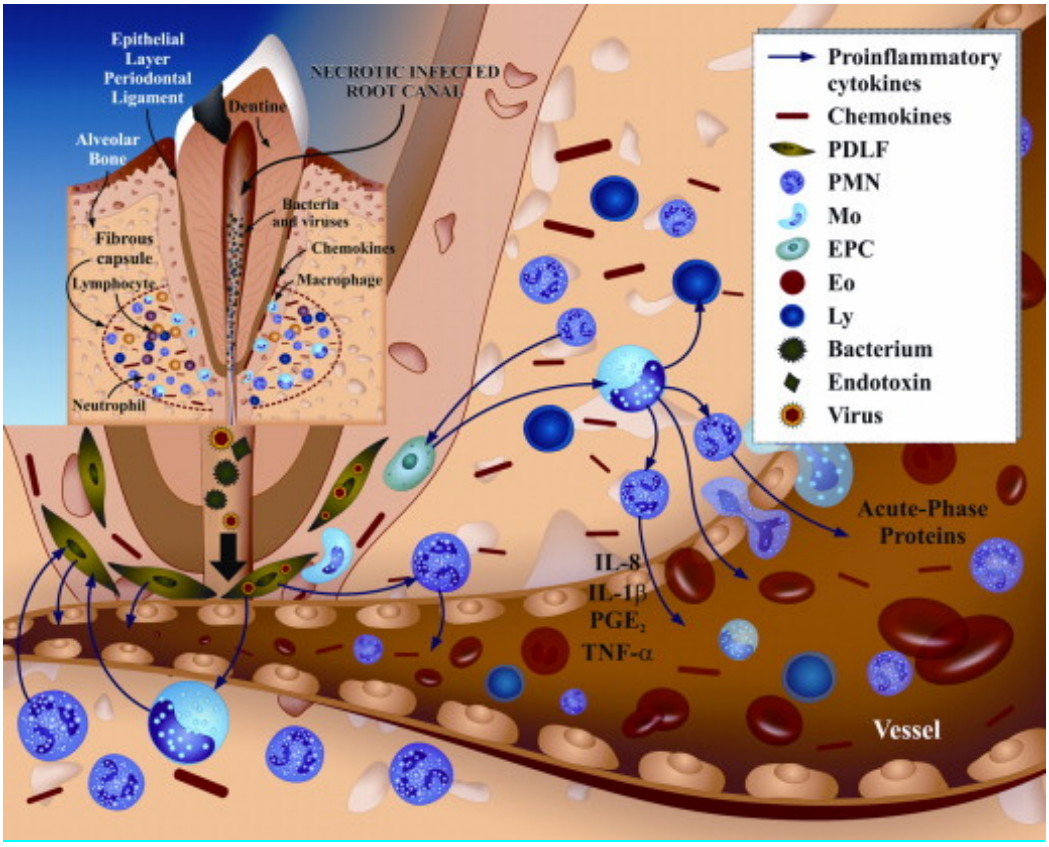
Ligands (L)	Cell type	Action	Action on pulp
		B cells, up-regulation of CD23 and IL-4R, survival factor for B and T cells, role in tissue adhesion and inflammation	
IL-6	Endothelial cells, fibroblasts, monocytes/macrophages	Synthesis of acute phase proteins; stimulates activation and trafficking of leukocytes; differentiation, activation, survival of T cells; B cell: differentiation and production of IgG, IgM, IgA; hematopoiesis	May stabilize the dimensions of chronic lesions; proinflammatory and anti-inflammatory effects; it increases in teeth with symptomatic pulpitis
IL-10	T cells, B cells, monocytes, macrophages, dendritic cells	Immune suppression	Inhibitory effect against bone resorption
IL-12A, B	Monocytes, macrophages, neutrophils, microglia, dendritic cells, B cells	Induce T_H1-cell differentiation and cytotoxicity	Correlations to bone-resorptive processes
IL-13	T cells, NKT cells, mast cells, basophils, eosinophils	Switching to IgG4 and IgE; up-regulation of CD23, MHC-II on B cells; induction of CD11 b, CD11c, CD18, CD29; CD23, and MHC-II on monocytes; activation of eosinophils and mast cells; recruitment and survival of eosinophils	Inhibits resorption
IL-17	T cells	Induces production of IL-6 and -8	Induces IFN-γ production; increases production of CXCL1 and CXCL5 chemokines
IL-18	Macrophages, astrocytes, Kupffer cells, keratinocytes, osteoblasts, dendritic cells	Induction of IFN-γ in presence of IL-12; enhances NK cell cytotoxicity; promoting T_H1 or T_H2–cell responses depending cytokine enviroment	Proinflammatory effects, similar to IL-12
IFN-γ	$CD8^+$ and $CD4^+$ T cells, activated NK cells	Activation of macrophages; induces MHC class II protein expression; inhibits IL-4dependent class II expression on B cells; regulates TH1 cells development; regulates immunoglobulin class switching	Proinflammatory effects, might have a crucial protective effect on the pathogenesis of late periapical bone resorption*in vivo*
TNF-α	Macrophages, monocytes, astrocytes, B cells, basophils, cardiac myocytes, eosinophils, fibroblasts, glial cells, granulosa cells, keratinocytes, mast cells, neurons, neutrophils, tumor cells	Cell cytotoxicity; improvement of the function of NK cells; fever; anorexia; essential role in septic shock	Promotes bone resorption; protective role against spread of infection
LT-α (TNF β)	NK, T, and B cells	Mediates inflammatory, immunostimulatory and antiviral responses; plays a role in apoptosis	Proinflammatory effects

Ig, immunoglobulin; IL, interleukin; NK, natural killer; NKT, natural killer T cells.

Pathogenesis of apical periodontitis (Courtesy of Frederico C. Martinho 2015 JOE)

T lymphocytes are one of the key elements involved in apical periodontitis, considered the major sources of cytokines. These cells bear antigen-specific receptors on their cell surface to allow recognition of foreign pathogene. There are 2 main subsets of T lymphocytes distinguished by the presence of cell surface molecules known as CD4 and CD8. T lymphocytes expressing CD4 are also known as helper T cells 1 and 2, and these are regarded as being the most prolific cytokine producers. This subset can be further subdivided into Th1 and Th2, and the cytokines they produce are known as Th1-type and Th2-type cytokines. The progression of apical periodontitis and consequent bone destruction have been attributed to the earlier onset of Th1 response inducing differentiation and activation of osteoclasts by nuclear factor kappa B ligand (RANKL). On the other hand, the healing process seems to be related to the later onset of Th2 response. Th1 cells tend to produce a proinflammatory response such as interferon (IFN)-γ, interleukin (IL)-2, and tumor necrosis factor (TNF)-β. Meanwhile, the Th2-type cytokines include cytokines IL-4, IL-5, and IL-13. Interestingly it was shown that all irrigation protocols (CHX, CaOH, CaoH+CHX) are effective in significantly lowering the levels of Th1-type cytokines. Both Ca(OH)2 medications significantly increased the levels of Th2-type cytokine. CHX medication showed the lowest effectiveness in increasing the levels of Th2-type cytokine.

Overlapping Protective and Destructive Regulatory Pathways in Apical Periodontitis **(From Ildikó J. Márton 2014 JOE)**



"A schematic representation of the regulation of the initial inflammatory cell responses in the periapical area. The interaction of LPS and TLRs expressed on PDL fibroblasts (PDLFs) initiates the production of proinflammatory cytokines and chemokines IL-8/CXCL8, MCP-1/CCL2, RANTES/CCL5, pro-IL-1β, IL-6, stromal-derived factor 1, and TNF-α as well as the immunoregulatory compounds TGF-β, IL-1Ra, and sTNF-αR. Proinflammatory mediators induce vasodilation and attract PMNs and MNPs to the periapical area. Invading bacteria, their byproducts, and the first wave of inflammatory mediators activate phagocytes. These cells produce a broad set of soluble mediators, which destroy pathogenic microbes, injure tooth-supporting tissues, and attract further cells of the innate and adaptive immune system. In contrast, immunoregulatory compounds attenuate the intensity of inflammatory reactions and host tissue destruction".

Frederico C. Martinho (JOE, 2014) investigated the signaling pathway activation by primary endodontic Infectious contents and production of Inflammatory mediators. "It has long been known that primary endodontic infection has a polymicrobial etiology caused by both gram-positive and gram-negative anaerobic bacteria. The latter have lipopolysaccharides (LPSs, known as endotoxins) located on the outer layers of bacterial cell walls and are considered one of the major factors involved in the inflammation response. LPSs have been shown to interact with Toll-like receptors (TLRs), both TLR-2 and TLR-4, but with greater affinity for TLR-4 which in turn recognizes the LPS molecule and activates multiple downstream signaling pathways. The binding of LPSs to TLR-4 leads to the activation of p38 mitogen-activated protein kinase (p38 MAPK) (an upstream effector common to many inflammatory cytokines) and NF-ϰB transcription factor (central to several immune and inflammatory responses), which are responsible for proinflammatory cytokine production, such as interleukin (IL)-1 beta, tumor necrosis factor alpha, prostaglandin E2, and IL-6 and -10. It was shown that IL-6 levels from cell cultures stimulated with material from teeth with tenderness to percussion were significantly higher than in its absence. Thus, a higher level of IL-10 was found in macrophage stimulated with contents from teeth with pain on palpation than in those without it. Relatively higher levels of IL-6 and IL-10 were found when macrophages were stimulated with contents from teeth showing a radiolucent area ≥2 mm compared with those <2 mm. Correlations were found between endotoxin contents and levels of IL-6 released in the culture media after cell stimulation.

Kakahashi, Stanley, & Fitzgerald (1965 P 340-349 OOO Volume 20):
36 rats, 21 germ-free (Gnotobiotic) and 15 Conventional. Using half round carbide burs on first maxillary molars. Day 14: Sterile pulp showed dentin bridging while the others showed necrosis.
Endodontic infection is caused by bacteria/ in the absence of microorganism there is no endo infections.

Moller has the main step study in microbiological study analysis of root canals. Monkey study show that in devitalized non infected tooth there is no PA lesion. He also refused the anachoresis by showing that sterile necrotic pulps remained aseptic.

Bergenholtz in 1974 talked about the etiology of Periapical lesion:
Facultative -> anaerobes -> LPS, toxins -> host response -> osteoclasts -> lesion. It was shown that Bacteria required to cause PA lesion.

Love (1996) in a laboratory experiment indicated that bacteria can enter through even minor cracks in enamel and dentin following trauma.

Berman & Kuttler (2010 JOE): When a tooth has no significant restorations or caries, whereby the pulp is nonvital in the absence of a luxation injury, it is suggested that this necrosis is likely caused by a significant longitudinal crack that extends from the occlusal surface and into the pulp. This type of presentation has been termed **"fracture necrosis."**

Bernick (1977) talked about effect of aging on the nerve supply to human teeth. He also proved the presence of lymphatic vessels inside the pulp. Aging increase the incidence of pulp stone. Pulp stone form due to calcification of pulp contents like collagen that act as nidus.

Van Hassel (1989) disproved the strangulation theory. Vascular effects are localized in the low compliance environment and do not effect the whole pulp.
What is strangulation theory? As pulpal inflammation ↑, pulpal pressure ↑. With this increased pressure, veins and lymphatics collapse at the apex and strangle the pulp - necrosis results. Tonder in a cat study disproved this theory; localized increase in pressure with no strangulation

Izumi (1995) discussed varying levels of inflammation. Adaptive immune response occur in irreversibly inflamed pulps separated by less than 2mm from a deep carious front.
1. enamel caries – increased T cells; little or no B, plasma, PMN
2. dentin caries – dramatic T/B cell and PMN increase
3. to 0.5 mm pulp – increase PMN, macrophages, plasma cells, B cells
4. w/in 0.5mm – micro-abscesses formed, decrease in pulp cells and loss of ECM

Taylor & Byers: Injury causes neural spouting & increased release of substance vasoactive amins like P and CGRP (Neuropeptides can cause neurogenic inflammation), which cause vasodilation (control pulp blood flow), and release of inflammatory agents. This finding was also confirmed by **Hargreaves** who declared that Sensory nerves may thus play a role in instant defense reactions of the pulp. **Taylor** also showed that innervated teeth have less pulp necrosis and PA destruction than denervated.

The presence and over expression of substance P in human dental pulp and periodontal ligament when teeth are submitted to occlusal trauma shows the effect of occlusal interferences on PDL inflammation and tenderness. Also heavy orthodontic forces showed over expression of CGRP and pulpal inflammation. Therefore, CGRP expression in human dental pulp increases when teeth are submitted to severe orthodontic forces **(Javier Caviedes-Bucheli, 2011 JOE).**

Matthew's Sequence: Stimulation of the dentin tubules ⇒fluid movement ⇒stimulation of sensory nerves in the subodontoblastic plexus⇒release of vasoactive amines like SP and CGRP⇒ vasodilation and increased pulpal pressure in the localized area⇒axon reflex mechanism⇒fluid movement outward to decrease the intra-pulpal pressure.

KIM (JOE, 1990): Pulp is in low compliance system. The two main mechanisms in the inflammatory response of pulp are circulation and sensory nerve. Excitation of A-delta has no effect on the circulation but C fibers excitation cause release of substance P which can cause vasodilation and affect the pulp blood flow. Also vasculature of the pulp contains adrenergic receptors that sympathetic excitation can alter the PBF.

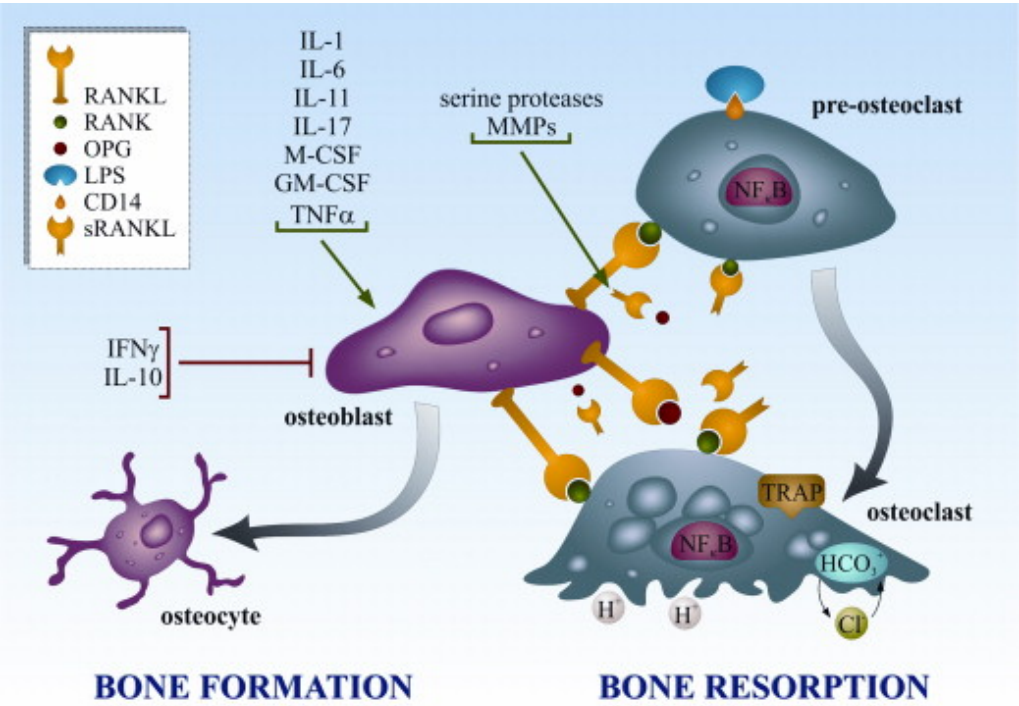
Gomes (2012, JOE) reviewed the cytokines involved in pulpo-periapical disease. "The inflammatory process is initiated and maintained by the emergence of a network of chemokines (eg, interleukin [IL]-8) and proinflammatory (eg, tumor necrosis factor α [TNF-α], IL-1β, and IL-6]) and anti-inflammatory mediators (eg, IL-10, IL-1 antagonism, and IL-4) that play distinct or shared biological activities. TNF-α stimulates the production of collagenase, prostaglandin E2 (PGE2), chemo- and cytokines, cellular adhesion molecules, and bone resorption–related factors. IL-6 acts as a proinflammatory cytokine during periodontitis and stimulates osteoclastic differentiation and bone resorption in chronic inflammatory periodontitis. PGE2 can induce or repress IL-6 and vice versa. Conversely, IL-10, which is produced by both innate and adaptive immune cells, controls and suppresses the inflammation in order to down-regulate the adaptive immune reaction and minimize tissue destruction in response to microbial challenge" **(From Takigawa Seymour and Boyce studies).**

Stashenko studied the sequence of bone lesion formation in a rat model: Bone resorption is mainly due to IL-1 alpha, IL-1 beta, TNF, PGE2 which is called osteoclastic activation factor. OAF are the main cause of bone lesion formation rather than direct effect of LPS. (**Torabinejad** showed that inhibition of PGE2 using indomethacin can reduce the bone resorption in cat model). PGE2 can be produced by macrophages and fibroblasts. **Stashenko** also in a study with Rats and PGG glucan (enhances circulating neutrophils) showed the significant role of neutrophils and monocytes in limiting the disease process. Less necrosis with PGG glucan enhanced rats for 20 days. It was also suggested that during early phase helper T-cells (CD4+) predominate and during chronic phase cytotoxic T-cells (CD8+) predominate.

Torabinejad talked about high concentration of leukotriene B4 (produced in lipoxygenase pathway) in symptomatic human periapical lesions.

Fukagawa et al 2002 showed the periapical bone lesion formation sequence.
-RANK surface receptor on Osteoclast precursor cells
-RANKL-RANK binding --> active osteoclast --> bone resorption
-Osteoblast when active express and secrete OPG osteoprotegerin which act as a decoy receptor and inhibits RANKL-RANK interaction and thus bone resorption.
-Hormones and cytokines exert their effects largely by influencing RANKL-RANK interaction directly or by changing the ratio of RANKL-OPG reciprocal gene expression.

The equilibrium between bone formation and resorption is regulated by the interaction between osteoblasts and osteoclasts and their precursors **(Courtesy of Ildikó J. Márton 2014 JOE)**



Membrane-bound RANKL expressed in osteoblasts stimulates the differentiation of osteoclast precursors and the bone-resorbing activity of mature osteoclasts through interaction with its receptor RANK. The soluble form of RANK, OPG, inhibits RANKL-RANK interaction. RANKL-RANK signaling activates nuclear factor-κB. Osteoclasts are descendants of the bone marrow–derived monocyte/macrophage lineage and are characterized by the expression of tartarate-resistant acid phosphatase (TRAP). The osteoclast releases hydrogen ions (H+) through the action of carbonic anhydrase, resulting in a low pH environment in the bone-resorbing lacuna. Bicarbonate (HCO3−)-chloride (Cl−) ion exchange restores the intracellular pH of this cell. The expression of RANKL and OPG is reciprocally regulated by IL-1, IL-6, IL-11, IL-17, M-CSF, GM-CSF, and TNF-α, which

induce bone resorption. RANKL is an additional stimulator of bone resorption. LPS may contribute to the differentiation of osteoclast precursors. In contrast, IFN-γ and IL-10 decrease the RANKL-OPG expression ratio and attenuate bone resorption. In the bone formation process, osteoblasts differentiate into osteocytes.

Zhang (JOE, 2015): "A proper balance between osteoblastic and osteoclastic activities is crucial for bone structure and function. Elevated osteoclast activity results in inflammation-mediated bone diseases, such as periapical lesions, periodontal diseases, osteoporosis, and rheumatoid arthritis (**Walsh et al. 2005**). Osteoclasts are multinucleated giant cells, originating from haemopoietic progenitors of the monocyte–macrophage lineage and resorbing mineralized tissues. Macrophage colony stimulating factor (M-CSF) and receptor activator of nuclear factor-jB ligand (RANKL) are critical cytokines that contribute to the differentiation and function of osteoclasts (**Takayanagi 2007**). Traditional MTA has recently been reported to attenuate osteoclast differentiation and function (**Hashiguchi**)".

Nair: IL-1a, TNF, PG from macrophages; rapid bone resorption 7-20 days, slow thereafter.
Main resorption from pro-inflammatory host-derived substances, minimal effect from bacterial components which is called a dynamic encounter between root canal infection and host response. Along with bone resorption, some apical parts of the root will be lost as well. Often just visible only in microscopic sections.

Torneck: Odontoblasts for a physiological barrier between dentin and pulp in adult teeth. This barrier is perturbed following routine restorative procedure. It was concluded that following carious exposure, the unmyelinated nerve axons (C fibers) appeared to be least affected.

Mast cells can be detected in both inflamed and uninflamed pulp tissue **(Farnoush JOE 1984)**

Olgart 1990; Gazelius 1987: **Neurogenic inflammation** is a key vascular mechanism in response to injury (activates T lymphocytes, SP, CGRP,…).

Branstrom & Lind 1965: Pulpal responses occure quite early in enamel caries.

Reeves & Stanley 1966: Caries into dentin⇒0.5mm remaining dentin may lead to healing; only once reparative dentin is invaded⇒ irreversible pathosis. Also **Stanley 1981** reported that 1mm of dentin reduces toxic effect of material to 10% of the original level. 2mm of dentin completed blocks pulpal response to a toxic material.

Bergenholtz and Linde 1975: Cl V cavity + plaque in monkey ⇒ ⇑vascular permeability⇒migration of inflamed cells.

Trowbridge 1981; Bergenhlotz 1990: Pulp tissue reacts to caries long before bacteria reach pulp.

Hahn, Liewehr 2007 (JOE) assessed the relationship between pro-inflammatory and anti-inflammatory cytokines from bacteria caries
High Lactobacilli: IL-10 (anti-inflam)⇒no sensitivity
Low Lactobacilli / High Prevotella: Indole/Ammonia⇒Heat sensitivity
Low Lactobacilli / High Streptococci: pre-inflammatory cytokines (TNF, IL-1)⇒Cold and Heat Sensitivity

Narhi elaborated the role of intradental A- and C-type nerve fibers in dental pain mechanisms: 1) A-fibres are responsible for the sensitivity of dentine and thus for the mediation of the sharp pain induced by dentinal stimulation, 2) Prepain sensations induced by electrical stimulation result from activation of the lowest threshold A-fibers some of which can be classified as A beta-fibers according to their conduction velocities. Comparison of the responses of the A beta- and A delta-fibers indicate that they belong to the same functional group, 3) Intradental C-fibers are activated only if the external stimuli reach the pulp proper. Their activation

may contribute to the dull pain induced by intense thermal stimulation of the tooth and to that associated with pulpal inflammation.

Tomoatsu Kaneko (JOE, 2010): Increased gene expression of Toll-like Receptors and Antigen-Presenting Cell–related molecules in the onset of experimentally induced furcation lesions of endodontic origin in rat molars: Messenger RNA expression levels of TLRs and the APC-related molecules in the furcal periodontal ligament were significantly up-regulated in teeth with unsealed pulpotomy. These results suggested the involvement of innate immune mechanisms involving TLRs and resulting activation of APCs in the early pathogenesis of pulp infection-induced furcal inflammation.

The inflammatory tissue present in periapical lesions is populated predominantly by macrophage (**Metzger, dental Tru, 2000**). Gram-negative bacterial LPSs are one of the mainly potent stimuli for macrophages cells in the release of PGE_2. PGE_2 is implicated in most of the inflammatory and destructive changes that occur in apical lesions, such as vasodilatation, increasing vascular permeability, collagen degradation, and bone resorption. The possible role of PGE_2 in the pathogenesis of apical periodontitis has been provided in endodontic literature (**Garrison, Torabinejad**). **Gomes (JOE, 2011)** showed that teeth with clinical symptomatology were related to higher levels of endotoxins and PGE_2 secretion.

Henriques (2011, JOE) investigate the pro-inflammatory cytokine predominates in refractory dental lesions. It was found that TNF-α, IFN-γ, IL-17A, and Monocyte Chemo-attractant Protein (MCP-1) mRNA are over expressed in the periapical immune response in cases of endodontic failure.

- **Matrix metalloproteinases** (MMPs), also called matrixins, are synthesized as latent enzymes that can be stored in inflammatory cell granules but are more often secreted and found anchored to the cell surface or tethered to other proteins on the cell surface or within the extracellular matrix. MMPs were initially classified as zinc-dependent proteinases capable of digesting the various structural components of the extracellular matrix. More recent work showed that they exhibit collagenolytic activity. Their specific proteolytic targets have since expanded to many other extracellular proteins. **Geraldine M. Ahmed in a 2013 (JOE)** study found that tooth with symptomatic apical periodontitis showed a significantly higher mean number of gram-negative cells ($P = .001$) and MMP-9 area percent ($P < .001$) than the asymptomatic group. Also **Johannes Mente (2016, JOE)** suggested that MMP-9 levels in pulpal blood samples could be a useful ancillary diagnostic tool for distinguishing different stages of pulp tissue inflammation as there is a significant difference betweene irreversible and reversible pulpitis regarding the MMP levels.

Are antibodies present in the pulp? Hahn suggested that igG is the major class of AB in the pulp. He said that these AB also present in healthy pulp indicator the role of humeral immune system in pulp defense. The amount of igG increase the inflamed pulp. **Nakanishi** also showed that the level of igG, igM and igA and PGE2 increased in the inflamed pulp.

3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins) are the first-line pharmaceuticals for the prevention and treatment of dyslipidemia. In a recent study by **Mary T. PettiettE (2013, JOE)** the potential correlation between statin and pulp chamber calcification was assessed. The significant increase of calcification and loss of vertical height of the pulp chamber observed in mandibular molars in patients on statin medication indicated a possible increased odontoblastic activity. Therefore, systemic statins could be a contributing factor for pulp chamber calcification.

Cellular adaptation to hypoxia depends on the transcription factor hypoxia-inducible factor (HIF) which is only activated in hypoxia condition. Hypoxia can change the inflammatory reaction. Following hypoxia, the metabolic pathways shift toward glycolysis which convert glucose to pyruvate and finally lactic acid using Lactate dehydrogenase. It has been shown that this change in metabolic pathway can induce apoptosis.

Infections induced bone loss predominantly results from an uncoupling of the activities of osteoblast and osteoclast. Beside promotion of osteoclast, apoptosis of osteoblast can induce the PA lesion (**Marriot, Mikhaeilof).**

In 2011, Khalid Merdad investigated the caries Susceptibility of Endodontically versus nonendodontically treated teeth and suggested that streptococcus mutans count, de novo plaque formation, and recurrent caries were higher on the surface of ETT compared with NETT. This finding was attributed to the fact that most of the ETT have big fillings. Surfaces of filling material might be more retentive for plaque because of surface roughness and differences in surface tension.

" **Tricalcium silicate cements** refer to a group of hydraulic cements with tri- and dicalcium silicates as their dominant ingredient, which react with water to form calcium silicate hydrate and calcium hydroxide. The application of these cements is abundantly being recommended for vital pulp therapy, and over the past decade, a field of research has emerged focusing on the modification or development of newer tricalcium silicate cements that could overcome the shortcomings of their predecessors and increase their clinical efficiency". **Elanagai Rathinam (JOE, 2015)** reviewed the molecular signaling of dental pulp cells in response to Tricalcium silicate cements. Biodentine, Bioaggregate, and mineral trioxide aggregate stimulate the osteogenic/odontogenic capacity of DPCs by proliferation, angiogenesis, and biomineralization through the activation of the extracellular signal regulated kinase ½, nuclear factor E2 related factor 2, p38, c-Jun N-terminal kinase mitogen-activated protein kinase, p42/p44 mitogen-activated protein kinase, nuclear factor kappa B, and fibroblast growth factor receptor pathways. When DPCs are placed into direct contact with tricalcium silicate cements, they show higher levels of gene activation, which in turn could translate into more effective pulpal repair and faster and more predictable formation of reparative dentin.

Specific signaling molecules related to the inflammatory response and the biomineralization process were analyzed to assess host-MTA interactions by **Reyes-Carmona (2010, JOE).** They suggested that MTA induced a time-dependent proinflammatory cytokine up-regulation up to 3 days. Immunohistochemical analyses showed an up-regulated expression of myeloperoxidase, nuclear factor-kappa B, activating protein-1, cyclooxygenase-2, inducible nitric oxide synthase, and vascular endothelial growth factor on day 1. Scanning electron microscopic examination revealed the presence of apatite-like clusters on collagen fibrils over the surface of tubes containing MTA.

Nair 1997/1998: cyst formation hypotheses:
1. The Nutritional Deficiency Theory:
As islands of epithelium expand, more central epithelial cells are distanced from their nutritional supply and undergo necrosis. A cystic cavity results in the center of the cell mass as liquefaction necrosis occurs.
2. Abscess Theory:
An abscess cavity is formed in the periapical connective tissues. Subsequently, the abscess is completely surrounded by epithelium because of the natural inclination of stratified squamous epithelium to line exposed connective tissue surfaces.
3. Merging of epithelial strands theory:
As epithelial strands continue to grow, they merge to form a 3D ball mass. When connective tissue trapped inside the ball mass degenerates, a cyst is formed.

Nair: Pocket cyst (**Bay cyst as defined by Simon**) can be healed by RCT. True cysts, particularly large ones with cholesterol crystals are less likely to resolve following RCT because these cysts are self-sustaining and they are independent of canal content. Also persistent intraradicular infection and presence of Actinomyces isrealii were reported as a result of failure and this might be due to its ability to build cohesive colonies that protect it against immune system. 50% granulomas, 15% cysts (61% of the cysts are true and 39% pocket cysts) and 35% PA abscesses consist periapical lesions (depends on study the incidence of cysts has been reported 6-55%). Cholesterol crystals are found in cysts (not granulomas). It should kept in mind that the prevalence of

true cyst are far less than 10% and we can expect too see that most of the lesions heal after RCT. **True cyst account for <10% of all periapical lesions.**

Rubinstein & Kim: Periapical lesions consist of 85% granuloma and 15% cyst.

Stern MH, Dreizen S, Mackler BF, et al. Quantitative analysis of cellular composition of human periapical **granulomas** (JOE 1981). The cellular composition of 33 solid and cystic periapical granulomas was quantitated by a differential morphometric technique. **Macrophages** were the predominant inflammatory cell, followed in descending numerical order by **lymphocytes**, **plasma cells**, and **neutrophils**. Inflammatory cells comprised slightly more than half the formed elements (52%); the others were connective tissue elements. There were no significant qualitative or quantitative differences in the inflammatory components of lesions differing in morphology (solid vs cystic), symptomatology (pain vs no pain), duration (less than one-year vs more than one year), and treatment (endodontic intervention vs no intervention). The human periapical granuloma thus reflects a complex of immunologic and nonimmunologic inflammatory reactions.

Torabinejad: Granulomas and cyst were stained for both T and B cells and T cells were greater in number.

Anita Aminoshariae (JOE, 2015): Association of Functional Gene Polymorphism with Apical Periodontitis: Based on the current evidence, biologic modifiers cannot currently be considered a cause of any endodontic pathology, but they might be considered as an additional risk factor placing endodontic patients at risk for certain periapical pathological processes.

Morsani et al 2011 JOE:
Specific genetic markers associated with increased IL-1B production may contribute to increased susceptibility to Persistent Apical Periodontitis.

Diagnosis and testing:

- American Board of Endodontics terminology for diagnosis is what we need
    - Normal
        - Normal response to cold meaning has no spontaneous pain and no lingering pain to other apparently normal healthy teeth.
    - Reversible pulpitis
        - A little more sensitive to cold than a normal control tooth, no linger, no severe sensitivity and no spontaneous pain.
    - Asymptomatic irreversible pulpitis
        - No spontaneous pain/ A clinical diagnosis based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing. Additional descriptors: no clinical symptoms but inflammation produced by caries, caries excavation, trauma.
    - Symptomatic Irreversible pulpitis
        - Lingering to cold compared to "apparently healthy teeth" A clinical diagnosis based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing. Additional descriptors: lingering thermal pain, spontaneous pain, referred pain.
    - Necrotic
        - No response to cold
        - No response to EPT
    - Previously treated and obturated with gutta percha
    - Periapical
        - Normal
            - Lamina dura should be intact and PDL should be WNL (1 to 1.5 mm from all the) not sensitive to percussion, no spontaneous pain, no swelling, no sensitive to palpation hyper occlusion and ortho can cause PDL widening
        - Asymptomatic apical periodontitis
            - Lamina Dura not intact
            - No swelling
            - lucenies
            - No pain on percussion
        - Chronic apical abscess
            - Sinus tract (basically asymptomatic)
            - Maybe sensitive to palpation
            - No swelling
            - No spontaneous pain
        - Symptomatic apical periodontitis
            - Tender to percussion.
            - Little to no radiolucency depending on which text book.
            - Non intact lamina dura
            - No swelling/ No sinus tract
        - Acute apical abscess
            - Necrotic pulp
            - Swelling
            - Percussion sensitivity/ palpation / bite test
            - Spontaneous pain
            - Tender to bite
        - Condensing osteitis (**Eliasson:** CO is pulpul origin and can be treated in 85% with RCT)
            - Radio-opaque lesion at the end of the root.
            - No swelling or sinus tract
            - Low grade chronic insult
                - An insulting agent, deep enough to irritate the pulp

Seltzer and Bender 1963: There is a poor correlation between clinical diagnosis and pulpal histology. Studies have shown that electric pulp test results are most accurate when no response is obtained to any amount of electric current.

Asma khan (JOE, 2014) evaluated the masking effect of Iboprofen on Endodontics vitality tests. It was shown that Ibuprofen affected testing values for vital teeth by masking palpation 40%, percussion 25%, and cold 25% on affected teeth with symptomatic irreversible pulpitis and symptomatic apical periodontitis. There was no observed masking effect in the placebo group on palpation, percussion, or cold values. When nonvital teeth were included, the masking effect of ibuprofen was decreased. However, little masking occurred with the bite force measurement differences. Therefore, it was concluded that analgesics taken before the dental appointment can affect endodontic diagnostic testing results. Bite force measurements can assist in identifying the offending tooth in cases in which analgesics "mask" the endodontic diagnosis

Baume 1970: Histology and clinical finding didn't correlate

Eli I Int Endod 1993: Dental anxiety: a cause for possible misdiagnosis of tooth vitality.

EPT false positive: Touching saliva, liquefactive necrosis, anxiety, Dens invaginatus
EPT False negative: Medication, restoration, EPT DOESN'T HAVE battery, trauma, open apex, calcification

EPT stimulate a-delta fibers which are the **last** fibers develop in the tooth.

Himani Garg (JOE 2015): Dental Pulp Status of Posterior Teeth in Patients with Oral and Oropharyngeal Cancer Treated with Concurrent Chemoradiotherapy: Radiotherapy decreased the number of teeth responding to pulp sensitivity testing after doses greater than **30–35 Gy**.

King & King: It was reported that the EPT could be used effectively with the operator wearing latex gloves, but higher readings were obtained

Andre Mickel: Electric pulp tester conductance through various interface media. Of nonliquids, K-Y Brand UltraGel and Crest Baking Soda & P eroxide Whitening Tartar Control toothpaste recorded significantly ($p<0.05$) higher voltage readings.

Myers JW (1998) Demonstration of a possible source of error with an electric pulp tester **(JOE)** Adjacent tooth can pass and transmit the electricity and cause false positive.

Wahab and Kennedy talked about how rate of current raise in EPT affects sensation. Slowly increasing is more reliable 2 mu a/sec.

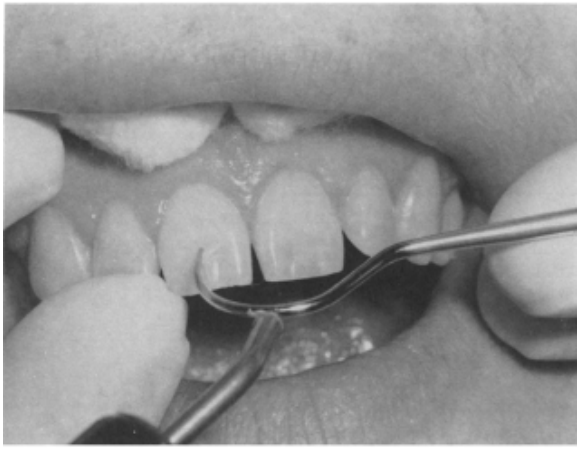
Seltzer & Bender (1963): Negative EPT ⇒Complete or partial necrosis 97.7% of the time.

Jacobson: The middle third of the incisors and the occlusal third of the posterior teeth were shown to have the least resistance. Place the EPT probe tip there!!

Rappaport and Bhaskar: Trauma teeth may have a false negative response with EPT and **we should wait** until response unless there are symptoms indicative of necrosis. **Trauma may change the nerve supply without altering blood supply.**

Andreasen: EPT is **unreliable** after trauma. EPT is not reliable in **immature apex** after trauma (May cause false +). **Cold is better in this situation.**

Anderson and Pantera (JOE, 1991): Bridging technique EPT in case of full coverage



Messerus & Trope suggested **Pulse Ox** as a reliable vitality test.

Kely Firmino Bruno (JOE, 2014) stated that the median oxygen saturation in normal dental pulps of permanent central incisors, lateral incisors, and canines was higher than **87%.**

Evans: laser doppler flowmeter. It was found that **LDF** can be an accurate, reliable, and reproducible method of assessing pulpal blood flow.

In medical diagnosis, test **sensitivity** is the ability of a test to correctly identify those with the disease (true positive rate), whereas test **specificity** is the ability of the test to correctly identify those without the disease (true negative rate).

Petersson (1999 EDT): Compared cold test (ethyl chloride), heat test (GP) and EPT (Analytical Tech) vs Gold Stnd (access and eyeball) for vitality. N=59. Petersson's results are as follows: Probability of negative test being necrotic pulp: 89% cold test, 88% EPT and 48% hot test Probability of positive test being vital pulp: 90% cold test, 84% EPT and 83% hot test.

Chavez (2013, JOE): talked about sensitivity and specificity of different diagnostic test. Cold test was the most accurate method of diagnostic testing. **Predictive values of thermal and electrical dental pulp tests: a clinical study. Sensitivity of Cold=88% hot=86% EPT=76%**

White and Cooley 1977: dichlorodifluoromethane and hot water give the largest temperature change

Jones, Rivera, Walton: talked about 1,1,1,2 tetrafluroethen (-26) as a cold test.

Jones: NSD between Endo ice and CO2. Also **large cotton pellet is better than a tip of cotton.**

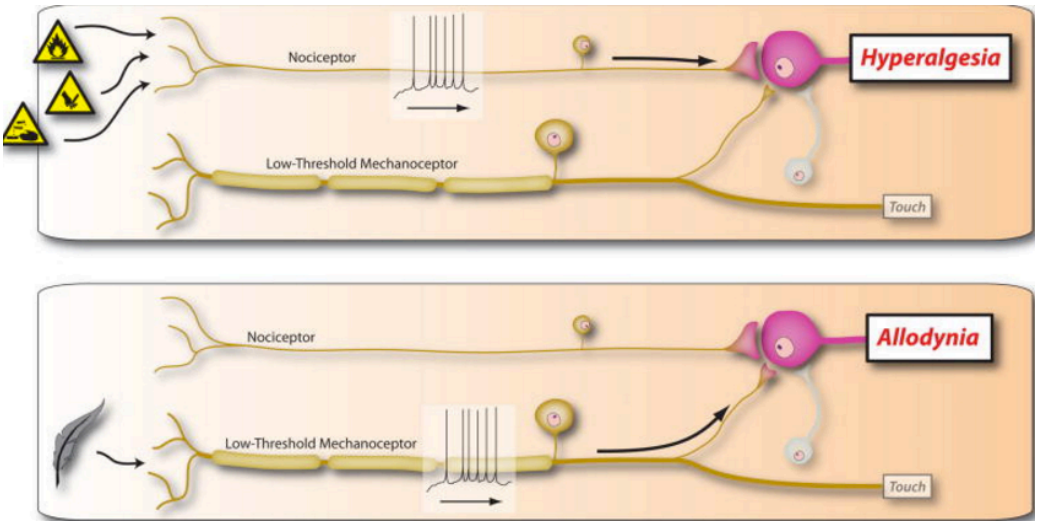
Trowbridge: Heated GP or CO2 showed **no pulpal injury** if used for clinically relevant duration

Keir and Schindler: Cases of sensitivity to hot after RCT due to missed canals. Heat testing can identify the last stages of disease and irreversible pulpitis.

Peters and Baumgartner: A multirooted tooth with one vital root may respond to a cold test (even in teeth with lesion).

Two of the most commonly used terms in the pain research and medicine world are **hyperalgesia** and **allodynia**. The word **hyperalgesia** means an increased response to a painful stimulus. The word **allodynia** means a painful response to a normally innocuous stimulus. Hyperalgesia = cold test AND alodynia= percussion test

Clifford J Woolf (Journal of pain, 2011):
The "referral pain phenomenon" is the concept of the attribution of pain to an anatomic region that is different from the location of the etiologic process. It is an effect of central sensitization. Referred pain from a tooth is usually provoked by an intense stimulation of pulpal C fibers the slow conducting nerves that when stimulated cause an intense, slow, dull pain.
Central sensitization: With the induction of central sensitization in somatosensory pathways with increases in synaptic efficacy and reductions in inhibition, a central amplification occurs enhancing the pain response to noxious stimuli in amplitude, duration and spatial extent, while the strengthening of normally ineffective synapses recruits subliminal inputs such that inputs in low threshold sensory inputs can now activate the pain circuit. The two parallel sensory pathways converge.



Friend and Glenwright talked about **referred** pain. Pulpal pains are difficult to localize. Anterior teeth don't usually refer posteriorly but posterior teeth can refer anteriorly. Posterior refer to opposing but anterior don't. **Patients can point out which tooth in SIP in only 37% accurate**; usually tooth to either side; 3.4% referral to opposite jaw; 1.5% referral across midline.

Okeson 1995:
Referred pain, often in a vertical pattern (arch to arch)
Consider selective anesthesia as additional dx tool
If local anesthesia at the site of pain fails to reduce pain, consider referred pain

Bender and Seltzer: anterior doesn't refer. Posterior may refer to opposite arch but not to anterior teeth. Mandibular teeth refer to periauricular area.

Van Hassel: when second molars were stimulated with an electric pulp tester, patients could discriminate

accurately which arch the sensation was coming from only 85% of the time, compared with an accuracy level of 95% with first molars and 100% with anterior teeth. When patients first feel the sensation of pain, they are more likely to accurately discriminate the origin of the pain. With higher levels of discomfort, patients have less ability to accurately determine the source of the pain. Therefore, in cases of diffuse or referred pain, the history of where the patient first felt the pain may be significant. Maxillary localization is better than mandibular.

The results of Patrick J. McCarthy study (2010, JOE) showed that patients presenting with odontogenic pain can localize the painful tooth **73.3%** of the time. Patients experiencing **periradicular pain can localize the painful tooth (89%) significantly more** often than patients with pain without periradicular symptoms. The presence of periradicular pain increases the accuracy of pain localization.

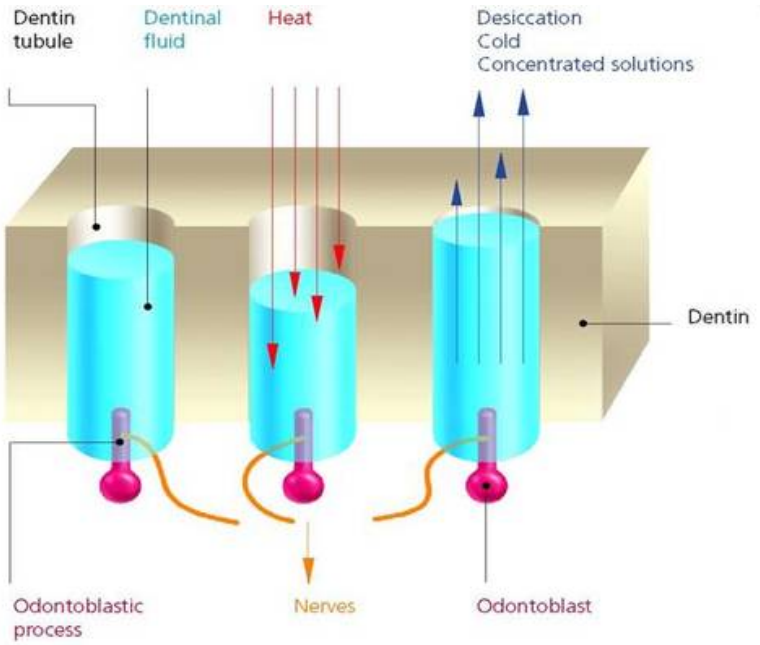
Pain can be better localized when the infection spread from pulp to periapical tissue due to presence of proprioceptive nerves.

Irreversible pulpitis with normal periapex probably has the highest number of referred pain!

Hydrodynamic theory:

- Early reports (**Anderson** 1963; 1961; 1967) have indicated that hypertonic solutions can induce fluid flow in dentinal tubules which was related to the osmotic pressure.
- Evidence obtained by **Olgart** (1974) and **Narhi** et al. (1982), that the ability of hypertonic NaCl to elicit INA increased with increasing cavity depth.

Brännström et al. 1967: Heat causes inward fluid movement; cold outward movement ⇒distortion of odontoblastic processes stimulates nerve response. Heat causes inward fluid movement in tubule and cold causes outward fluid movement.



Abou-Rass 1982: The **stressed pulp condition** is a clinical concept that describes pulps that have received repeated previous injury and survived with diminished responses and lessened repair potentials. Before

performing restorative dentistry, the dentist should conduct a comprehensive pulpal health evaluation on teeth to be restored.

Felton & Madison: 13% incidence of pulp necrosis following full crown coverage.

V. S. Dawson (IEJ, 2015) in a systematic review assessed the endodontic complications in teeth with vital pulps restored with **composite resins**: included studies reported few, if any, endodontic complications after composite restorations. Little or no differences emerged between teeth restored with composite resins and those restored with amalgam. To determine whether composite resin restorations of teeth with vital pulps are associated with an increased risk for development of endodontic complications such as apical periodontitis, further evidence is needed, from well-constructed studies with a large number of participants.

Bergenholtz 1984 (Human longitudinal study): Pulpal necrosis including periapical lesions developed with a significant higher frequency in **abutment** teeth than in non-abutment teeth.

In experimental studies, adverse cellular responses to resin composite material and dentin bonding agents have been observed in dental pulp cells (Galler, J Den Res). However, the periapical status of non–root-filled teeth with resin composite, amalgam, or full crown restorations has never been assessed in a retrospective study. **Victoria Dawsons (JOE, 2014)** stated that there is **no significant** difference in the frequency of apical periodontitis (AP) between teeth restored with resin composite or amalgam (1.3% and 1.1%, respectively). The frequency of AP for teeth restored with laboratory-fabricated **crowns was significantly higher** (6.3%). **Regression analysis showed no association between AP and resin composite restorations but a significant association with laboratory-fabricated crowns.**

Radiographic interpretation:

Goldman, Pearson and Darzenta (1972): Radiographs are **unreliable** (inter and intra agreement) 1972 & who's reading the radiograph 1974: 47% (less than half) of times did the examiners agree with each other and 72-88% of the times did the examiners agree with themselves after 6 months.

Brynolf (1967): multiple angle radiographs
2 additional radiographs increase the **diagnosis acumen** from 73% to 87% (3 radiographs).

Brynolf 1967 (Histologic Vs. Radiographic healing): This study was performed on human cadavers with X-rays taken of 320 upper incisors. Even though many radiographs appeared normal, complete histological healing after NSRCT occurred in **only 7%** of cases. Thus, radiographic success doesn't correlate with histological success. Also she suggested that the extend of histological inflammation is always bigger than what we see in radiographic case of apical periodontitits. This study is in **contrary with Green, Walton, 1997** who compared radiographic findings of NSRCT to histological exam of human cadavers. 74% of the teeth with normal radiographic findings showed NO inflammation. 26% with a normal periapex radiographically showed histologic signs of inflammation. The results of this study do not agree with those by Brynolf who found inflammation in the majority of the teeth that had received root canal treatment.

Seltzer & Bender: In order to detect a radiolucency in the radiograph 1) Erosion of the inner cortical plate 12.1% (volum bone loss); 2) 6.6% is mineralized bone loss; 3)7.1% soft tissue loss. If the root of a nonvital infected tooth is closer to the cortical bone (e.g., the mesial root of a mandibular first molar), the pathosis will be detected sooner than if the infected root is more centered within the cancellous bone (e.g., the distal root of a mandibular first molar).
It is evident from these experiments that, by the methods ordinarily employed for taking roentgenograms, lesions in cortical bone can be detected roentgenographically only if there is perforation on the bone cortex, erosion from the inner surface of the bone cortex, or extensive erosion or destruction from the outer surface. Lesions in cancellous bone cannot be detected roentgenographically. The apparent cancellous destruction that is manifest on roentgenograms is really an erosion of the innermost surface of the bone cortex at the junction are between cortex and cancellous bone. No defect can be visualized beyond the junction area as it encroaches on the marrow spaces. A study of 558 endodontically treated molars revealed that more lower molars than upper molars exhibit areas of rarefaction. This variation may exist because the upper molars are encased in cancellous bone, hence the lesion cannot be readily visualized on roentgenograms. It could also be due to a greater caries incidence in the lower molars. Roentgenographic detection is not facilitated until expansion of the lesion with erosion of the innermost surface of the cortex occurs. However, roentgenograms cannot disclose whether the lesion is on the buccal or lingual side.

Brynolf 1967: Widening PDL, loss of lamina dura and mineral loss of bone are radiographic signs of apical periodontitis. Best predictors of pulpal disease are disruption and change in the size of the PDL space and bone trabeculation.

Kaffe and Gratt 1988 talked about Lamina dura lost in apical periodontitis. The pathosis may present merely as a widening or break in the lamina dura.

the most consistent radiographic finding when a tooth is nonvital and aid in periapical diagnosis are PDL width and lamina dura.

Schwartz (1981 JOMS): "The lamina dura is a layer of compact bone (Cribiform plate or alveolar bone proper) that lines tooth socket; Xray beams passing tangentially through the socket passes many times the width

of the adjacent alveolus and are attenuated by this greater thickness of bone; producing the characteristic "white line" radiopacity" (Glickman). Normal teeth may not have detectable LD due to angulation of central beam and tooth in socket.

Slowey 1974: Radiographic Aids in detection of extra root canals

1) Fast break (change in the lucency)
2) More than one PDL
3) Fuzzy apex
4) Off-center canal: when the root canal is filled even in the angled radiographs it should be center. The closer the canals more acute angel is required to separate root canals (Max PM2). So if the canal moved in the angled radiograph there are probably multiple canals.
5) If it's treated, dark line next to the file or root filling material.

Zachariason: overlapping of zygomatic arch and maxillary sinus over root apices (estimation of WL or detection of lesion in posterior maxilla is hardest due to superimposition of anatomic structure)

Tamse (OOO, 1980): overlapping of zygomatic arch on the upper maxillary molars therefore bisecting method is not reliable.

Eberhardt and Torabinejad (1992, Loma Linda): 5% of maxillary roots are in sinus. The apex of the **MB root of maxillary second molars** is closest to the sinus floor (mean 1.97 mm) but farthest from the buccal bony surface (mean 4.45 mm). The apex of the buccal root of the maxillary first premolar is closest to the adjacent lateral bony surface (mean 1.63 mm) but farthest from the floor of the sinus (mean 7.05 mm).

Forsberg: paralleling technique is more accurate in length determination vs. bisecting angle

Clarks 1909: SLOB rule

The following clues utilize the buccal object rule to localize an object:

Clue No. 1: Changing the horizontal angulation causes the images of roots to tilt in the same direction in which the x-ray beam is directed. This concept is applicable in all regions of the mouth.

Clue No. 2: Changing the horizontal angulation causes the images of buccal cusps to move horizontally, relative to the lingual cusps, in the same direction in which the x-ray beam is directed. This clue applies only to multicusped teeth.

Clue No. 3: Changing the horizontal angulation causes the images of buccal root apices to move horizontally, relative to the lingual root apices, in the same direction in which the x-ray beam is directed. This clue applies to the maxillary molar region.

Clue No. 4: Changing the horizontal angulation causes the Ushaped image of the zygomatic process of the maxilla to move horizontally, relative to the maxillary molar roots, in the same direction in which the x-ray beam is directed. This clue applies to the maxillary molar region.

Clue No. 5: Changing the horizontal angulation causes the image of the anterior border of the ramus to move horizontally, relative to the mandibular molars, in the same direction in which the x-ray beam is directed. This clue is applicable to the mandibular molar region.

Clue No. 6: When a routine periapical x-ray examination is performed, the horizontal angulation is changed mesially for each exposure to direct the x-ray beam through the interproximal surfaces of the teeth, starting with

the central incisor region and progressing back to the molar region. This clue applies to all regions of the mouth, provided the teeth are positioned normally.

Clue No. 7: The vertical angulation of the x-ray beam determines the length of a tooth's image when angular film positioning is utilized. Increasing the downward direction of the beam will shorten the images of the maxillary teeth, while increasing the upward direction will shorten those of the mandibular teeth. This clue is applicable in all regions of the mouth.

Clue No. 8: Changing the vertical angulation causes the images of the buccal cusps to move vertically, relative to the lingual cusps, in the same direction in which the x-ray beam is directed. This clue is applicable only to multicusped teeth.

Clue No. 9: Changing the vertical angulation causes the images of the buccal root apices to move vertically, relative to the lingual apices, in the same direction in which the x-ray beam is directed. This clue is applicable only to multirooted teeth.

Clue No. 10: Changing the vertical angulation causes the U-shaped image of the zygomatic process of the maxilla to move vertically, relative to the maxillary molar root images, in the same direction in which the x-ray beam is directed. This clue applies only to the maxillary molar region.

Clue No. 11: Changing the vertical angulation causes the image of the anterior border of the ramus to move vertically, relative to the image of the mandibular molars, in the same direction in which the x-ray beam is directed. This clue is applicable only to the mandibular molar region.

Clue No. 12: A vertical angulation change occurs whenever a given region is radiographed using two different technics.

Nair showed that higher % of PARL are detected in conventional film compared to digital radiographs. Films show higher specificity and sensitivity compared to digital (OOOO-2001).

Barbat & Messer (1998 JOE): Cadaver study: Compared conventional radiography to digital radiography for detection of artificial PARLs. Both could detect removal of lamina dura and cancellous bone. BUT lesions were largest and easiest to detect when removed cortical plate.

White and pharaoh: Up to **75%** reduction in digital radiographs compared to conventional radiographs

Bohay (OOOO, 2000): Sensitivity and **specify** of films are 0.65 and 0.78. Means that 35 % of PA lesions are missed and in 22% would be inaccurately diagnosed.

Lamus (2001): Compared the accuracy of Schick sensor with conventional films regarding WL measurement and found NSD.

AAE and AAOMR Joint Position Statement

The decision to order a CBCT scan must be justified by showing that the benefits to that particular patient outweigh the potential risks of exposure to X-ray radiation

C. Kruse (Systematic review, IEJ 2015): It can be concluded that although there is a tendency for a higher accuracy for periapical lesion detection using CBCT compared to two-dimensional imaging methods, no studies have been conducted that justify the standard use of CBCT in diagnosing periapical lesions. In addition, it should be considered that, at the present time, the efficacy of CBCT as the diagnostic imaging method for periapical lesions has been assessed merely at low diagnostic efficacy levels.

Kamile Leonardi Dutra (JOE, 2016) assessed the diagnostic accuracy of conventional radiography and cone-beam computed tomographic (CBCT) imaging on the discrimination of AP from no lesion in a **meta-analysis**. It was mentioned that the accuracy values were 0.96 for CBCT imaging, 0.73 for conventional periapical radiography, and 0.72 for digital periapical radiography. No evidence was found for panoramic radiography.

Mozza introduced CBCT 1998.

Velvart (2001) found **100%** accuracy with **CBCT** scans. All lesions diagnosed during surgery were also visible with the CT scan. However, when applying conventional radiographic imaging to these same cases, they found that only **78%** of these lesions could be detected.

Patel (2012): Diagnosis using CBCT revealed a lower healed and healing rate for primary root canal treatment then periapical radiographs. 123 teeth with 1 year follow up. Healed 92.7% for periapical radiographs VS 73.9% for CBCT. Same result was reported by **Rafael Fernández (JOE, 2013)** who reported the success outcome of endodontic treatment after 5 years in teeth with vital pulps **varied with each radiographic method**: 94.3%/periapical film radiograph, 92.3%/digital periapical radiograph, and 81.3%/CBCT.

Brady (2014-IEJ): The higher sensitivity and specificity of CBCT in detecting VRF. However, **Chavda** stated that DR and CBCT imaging showed similarly poor sensitivity of 0.16 and 0.27, respectively. Both imaging modalities had similarly high specificity of 0.92 and 0.83, respectively. There was no statistical difference between the diagnostic accuracy of either imaging modality. Fracture width did not affect the detection rate of either imaging modality.

In a systematic review and meta analysis, **Sangeeta Talwar (JOE, 2016)** provide evidence about the accuracy of CBCT imaging in diagnosing VRFs in human teeth with and without endodontic treatment compared with conventional/digital radiography. Results showed better sensitivity and specificity of CBCT scans than PRs in the detection of VRFs in unfilled teeth, particularly when a voxel size of 0.2 mm was used. Low pooled sensitivity and specificity of CBCT imaging was noted in detecting VRFs in endodontically treated teeth. It should be noticed that CBCT and PR has almost the same diagnostic odds ratio in detecting VRF in filled root teeth.

No difference in specificity was found, but there was a higher sensitivity using CBCT compared to digital radiographs (de Paula-Silva et al. 2009), meaning that PR and CBCT were equal in identifying healthy teeth, whereas CBCT identified more of the teeth with apical lesions

More periapical lesions were detected using CBCT compared to PR. The proportion of additional periapical lesions detected using CBCT varied from 10% to 4 times the proportion found with PR (**Lofthag-Hansen et al. 2007, Low et al. 2008, Christiansen et al. 2009, Bornstein et al. 2011, Liang et al. 2012)**

In **Balasundaram (2012)** study, the additional use of CBCT in relation to treatment planning was investigated (F&T-level 3). **No significant difference in treatment choice was found when additional information from CBCT was available**.

C. Kruse **(IEJ, SYSTEMATIC REVIEW 2015)**: Current information does not support a conclusion that the use of CBCT is beneficial for the patient. A few studies have evaluated whether the treatment plan changes when information from CBCT is available (F&T-level 3-4). Findings have, however, been inconclusive. Further, **no studies have evaluated whether the use of CBCT will affect the prognosis of the treatment (e.g. healing of the periapical lesion**).

F. J. Mota de Almeida (IEJ, 2015): The impact of cone beam computed tomography on the choice of endodontic diagnosis. The diagnosis changed in 22 patients (42%) between Stage 1(before CBCT examination) and Stage 2 (after CBCT examination). There were 28 changes in diagnoses amongst all teeth examined (35%).

Tadas Venskutonis (JOE, 2014) assessed the importance of CBCT in the management of Endo problems. It was stated that endodontic cases should be judged individually, and **CBCT imaging should be considered in situations in which information from conventional imaging systems may not yield an adequate amount of information to allow the appropriate management of endodontic problems.** CBCT imaging has the potential to become the first choice for endodontic treatment planning and outcome assessment, especially when new scanners with lower radiation doses will be available.

Edwin Chang (2016, JOE) and **Corbella (2014, OOO)** et al attempted to assess diagnostic ability of CBCT in VRF detection in both endodontically treated and non-endodontically treated teeth by separately analyzing both *in vivo* and *ex vivo* studies and concluded that because of a very limited number of studies and significant heterogeneity in study characteristics and reported outcomes, **there is currently no evidence to suggest that CBCT testing can provide any additional diagnostic benefit to VRF detection in teeth with endodontic treatment.**

Nair 2000: Along with bone resorption, some apical parts of the root will be lost as well. This finding was confirmed by **Wilcox** who showed that necrotic teeth with apical periodontitis had more apical resorption than teeth with normal apical tissue. **Always consider the possibility of root end resorption and open apex in cases with large lesions.**

Bashkar said you can't differentiate cyst and granuloma radiographically. **Trope (1989)** Used CT scan to differentiate cysts from granulomas. **However, Rosenberg (JOE, 2010)** concluded that CBCT imaging is not a reliable diagnostic method for differentiating radicular cysts from granulomas. Surgical biopsy and histopathological evaluation remain the standard procedure for differentiating radicular cysts from granulomas.

Delzangles proposed that teeth with granulomas showed apical resorption but cysts showed little or no resorption.

Natkin: Although not diagnostic, the presence of sclerotic border or lesions greater than 200 mm are usually cystic in nature.

I&D, Trephination and Sinus tract

When there is swelling, always perform incision & drainage!!
Hutter talked about decompression of cellulitis.
Benefits of incision and drainage:
(O) Oxygen, (I) increase circulation, (D) decrease bacteria count, (P) promotes healing, and (P) decrease pressure.

Infection overview (**From Dr.Krell's study guide**):

Fascial Space	Source	Borders
Buccal Vestibule	Any Mand tooth – exudates break through B cort. plate and apicies lie below attachment of Buccinator or Mentalis muscle	• Buccal cortical plate • Alveolar mucosa • Buccinator (post) • Mentalis (ant)
Body of the Mandible	Any Mand tooth – exudate has not perforated the periosteum "subperiosteal abscess"	• Buccal or lingual cortical plate • Periosteum
Mental Space	Mand anterior tooth – exudate breaks through the B cort. plate and apex lies below attachment of Mentalis	• Mentalis (superiorly) • Platysma (inferiorly)
Submental Space	Mand anterior tooth – exudate breaks through L cort. plate and apex lies below attachment of Mylohyoid	• Mylohyoid (superiorly) • Platysma (inferiorly)
Sublingual Space	Any Mand tooth up to 1 molar – exudates breaks through L cort. plate and apex lies above attachment of Mylohyoid	• Mucosa of floor of the mouth (superiorly) • Mylohyoid (inferiorly) • Mandible (lateral)
Submandibular Space (mild trismus)	Mand posterior tooth – exudates breaks through the L cort. plate and apicies lie below attachment of the Mylohyoid	• Mylohyoid (superiorly) • Platysma (inferiorly) • Mandible (lateral)
Pterygomandibular Space (Mdr/severe trismus)	Mand second or third Molars – exudates drains directly into the space or contaminated IAN block	• Medial Pterygoid (medial) • Ramus (lateral) • Lateral Pterygoid (superior)

Fascial Space	Source	Borders
Palate	Any Maxillary tooth with	• Palate (superiorly)

	apex near palate	• Periosteum (inferior)
Base of the Upper Lip	Maxillary Central Incisor with apex close to B cort plate & above attachment of Obicularis Oris	• Mucosa of the Base of the Upper Lip • Obicularis Oris (inferior)
Canine Space (Infraorbital)	Maxillary Canine or 1st Premolar – exudates breaks through B cort plate and apex lies above the attachment of the Levator Anguli Oris	• Levator Anguli Oris (inferior) • Levator Labii Superioris (superiorly)
Periorbital Space	Spread of infection from the Canine or Buccal Spaces	• Lies deep to the Orbicularis Oculi

Fascial Space	Source	Borders
Buccal Vestibule	Max posterior tooth – exudates breaks through the B cort plate and apicies lie below attachment of the Buccinator	• Buccal cortical plate • Alveolar mucosa • Buccinator (superiorly)
Buccal Space	Any Mand or Max posterior tooth – exudates breaks through B cort plate and apicies lie above/below the attachment of the Buccinator respectively	• Buccinator (medial) • Skin of Cheek (lateral) • Zygomatic arch/Buccinator attachment (superiorly) • Mandible/Masseter attachment (inferiorly)
Masseteric Space (severe trismus)	Impacted 3rd Molar	• Ramus (medial) • Masseter (lateral)
Temporal Space	Involved indirectly if an infection spreads superiorly from the inferior pterygomandibular or submasseteric spaces	Deep Temporal: • Skull (medial) • Temporalis (lateral) Superficial Temporal: • Temporalis (medial) • Fascia

Kelly and Ellinger 1988 (case report): Always trace sinus tract

"Sinus tract formation frequently occurs secondary to pulpal-periradicular disease. Although sinus tracts usually exit through the gingiva or the mucosa, they may also drain extraorally or through the gingival sulcus of the involved or an adjacent tooth. Those opening through the gingival sulcus may traverse a pathway directly through the periodontal ligament, or they may leave the alveolar housing and dissect subperiosteally to the osseous crest where they subsequently enter the gingival sulcus".

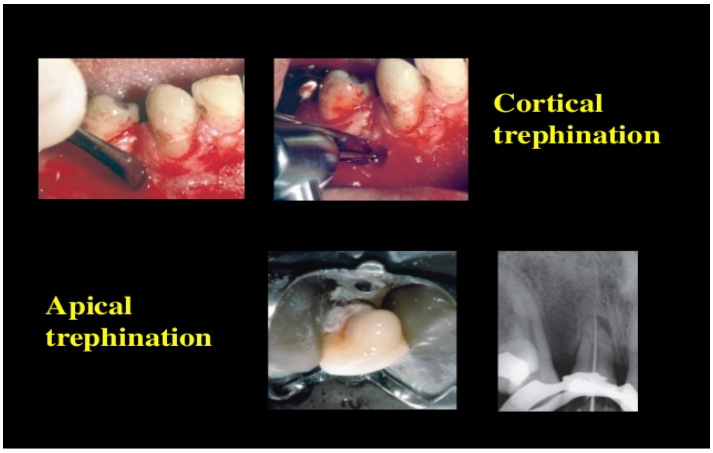
Larson suggested to trace sinus tract **with GP #25.**

Johnson presented five cases of facial lesions that were initially misdiagnosed as lesions of nonodontogenic origin. The correct diagnosis in each case was cutaneous sinus tract secondary to pulpal necrosis and

suppurative apical periodontitis. All facial sinus tracts resolved after the patients received nonsurgical root canal therapy. They concluded that if the sinus track is originating from odontogenic infection, the sinus track will be healed following NSRCT.

Harrison & Larson: most sinus tracts are not lined with epi and out of 10, **9 are lined with granulation tissue**.

Hasselgren G: establish **patency (apical trephination) to achieve derange** which helps to **relief the pain** especially in retreatment cases.



Arora M (2015-IEJ): Randomized clinical trial study- Maintenance of apical patency during chemomechanical preparation had no significant influence on post-operative pain in posterior teeth with necrotic pulps and apical periodontitis.

Dorn SO = In the absence of swelling, **trephination** is the surgical perforation of the alveolar cortical plate to release from between the cortical plates the accumulated tissue exudate that causes pain. Its use has been historically advocated to provide pain relief in patients with severe and recalcitrant periradicular pain

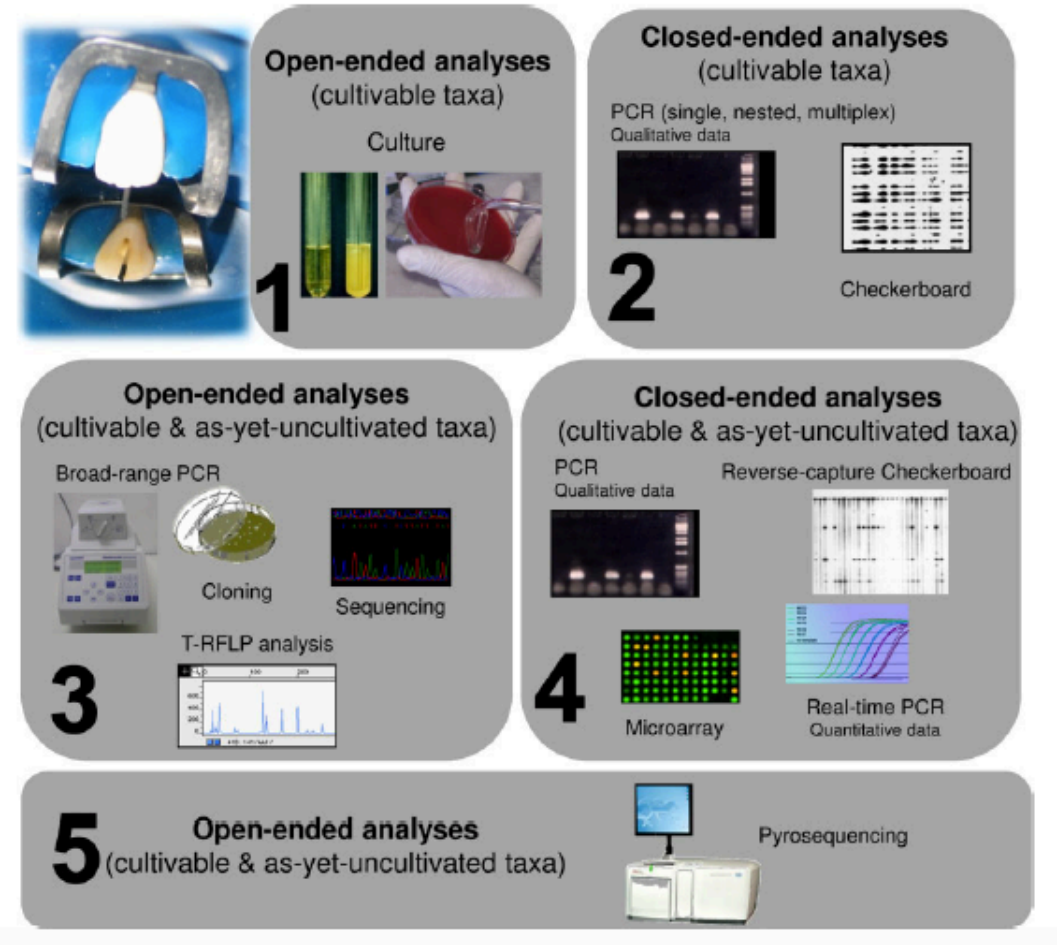
Moos HL: A comparison of pulpectomy alone versus pulpectomy with trephination for the relief of pain. They concluded that trephination was not effective in SAP.

Reader A: Effect of apical trephination on postoperative pain and swelling in symptomatic necrotic teeth. J Endod 2001: The purpose of this study was to evaluate postoperative pain and swelling after performing apical trephination in symptomatic necrotic teeth with apical radiolucencies. The apical trephination group took significantly less acetaminophen with codeine tablets. **Although the trephination procedure seemed to have some effect, there was no significant decrease in reduction of pain, percussion pain, or swelling and therefore its routine use is not recommended for symptomatic necrotic teeth with radiolucency**.

Microbiological studies:

History of microbiological studies:

Bergenholtz (JOE, 2015): "The culturing technique, based on samples from treated root canals, was a common method in the past to analyze the extent bacteria persisted in the root canal system after treatment. Although commonly taught and practiced in dental schools, the method never gained wide acceptance in the general practice of dentistry. An apparent reason was that culture methods are laborious to conduct, and it takes several days to weeks to identify anaerobic bacterial species. Furthermore, many species are not cultivable under laboratory conditions (This might explain why in most of the 70-80's studies there is no sign of anaerobic bacteria!!). On the other hand, culture-independent methods may identify these organisms. Yet, DNA-based identification methods such as polymerase chain reaction (PCR) suffer from high false-positive readings by the detection of DNA from dead bacterial cells. Recently, the detection of RNA by reverse-transcriptase PCR has been assumed to be a better alternative to DNA to measure viable bacteria. It is argued that RNAs are more labile and possess a shorter half-life than DNA, thus providing a better indicator of viable cells. However, the detection of viable bacteria by the reverse-transcriptase PCR method is also cumbersome and requires multiple processing steps as well as substantial laboratory instrumentation and setup".



"Cells in all organisms regulate gene expression by turnover of gene transcripts (messenger RNA, mRNA): The amount of an expressed gene in a cell can be measured by the number of copies of an mRNA transcript of that gene present in a sample. In order to robustly detect and quantify gene expression from small amounts of RNA, amplification of the gene transcript is necessary. The **polymerase chain reaction (PCR)** is a common method for amplifying DNA; for mRNA-based PCR the RNA sample is first reverse-transcribed to complementary DNA (cDNA) with reverse transcriptase".

"DNA–DNA hybridization generally refers to a molecular biology technique that measures the degree of genetic similarity between pools of DNA sequences. It is usually used to determine the genetic distance between two organisms. This has been used a lot in phylogeny and taxonomy. DNA–DNA hybridization is the gold standard to distinguish bacterial species, with a similarity value smaller than 70% indicating that the compared strains belong to distinct species. In 2014, a threshold of 79% similarity has been suggested to separate bacterial subspecies".

Sundqvist formula of infection: For endo infection to happen ⇒

$$\frac{\textit{Number of microorganism} \times \textit{Virulence factor}}{\textit{Host immunity}}$$

The only thing we can do following RCT is that we reduce the number of microorganism.

Sundqvist reviewed the Bacteria present in the root canal:

gr – anaerobic rods= Prevotella, Porphyromonas, Fusobacterium
gr – anaerobic cocci= Veillonella
gr + anaerobic rods= Eubacterium, Aa
gr + facultative rod= Lactobacillus
gr + anaerobic cocci= Peptostrep
gr + facultative cocci= Strep

Siqueira (2011, JOE) performed a very detailed study on the prevalence of different taxa in different Endo diagnosis. In teeth with asymptomatic apical periodontitis, the most frequent taxa were Dialister invisus (71%), Fusobacterium nucleatum (62%), and Porphyromonas endodontalis (62%). In chronic apical abscesses, the most prevalent taxa were P. endodontalis (100%), D. invisus (89%),Parvimonas micra (78%), and Solobacterium moorei (78%). In teeth with symptomatic apical periodontitis, the most prevalent taxa were D. invisus, P. endodontalis, S. moorei, Propionibacterium acnes, andStreptococcus species (all in 69%). None of the targeted taxa were significantly associated with either sinus tract or pain ($P > .05$), except for **Selenomonas sputigena**, which was more frequently found in painful cases ($P = .04$). No taxa were found in significantly higher levels in any conditions ($P > .05$).

Nair showed that the main difference between symptomatic and asymptomatic apical periodontitis are that on average the number of different species in one canal is lower in asymptomatic teeth.

Sundqvist (1992) used odds ratio analysis & concluded that bacterial pairings in infected RC systems are not random, but appear to be due to forces such as ecological commensalism. This finding was also reflected in **Fabricius** study who showed infections are organized **polymicrobial.**

Fabricius 1982 RC infections are **polymicrobial**. The pulps of 24 root canals, eight in each of the three monkeys, were mechanically devitalized and exposed to the mouth flora for about 1 week and thereafter sealed. Monkey teeth were left open for 1 week and then closed at various times. Relative # of obligate anaerobes increased over time.

Peptostreptococcus: gr+ strict anaerobic endo pathogen. Include 1) many (Magnus) 2) missing (Micros) 3) in (Intermedia) 4) action (Anaerobia).

Gomes (1994): 1) Pain is significantly associated with **Prevotella melaninogenica** and **Peptostreptococcus.** 2)Tenderness to percussion **Prevotella** or **anaerobes** and 3) Swelling associated with **Eubacterium** or with **Prevotella**. The idea that different bacterial species are associated with different clinical symptoms was also suggested by **Miller 1980** who said B.melaninogenicus is associated with sinus tract and pain.

Other gr+ strict anaerobic identified in infected root canals is **Actinomycosis**.

Proteolytic bacteria like Prevotella, Porphyromonas and Fusobacterium use necrotic tissue of pulp as nutrients. Prevotella and Porphyromonas contain a polysaccharide capsule which can protect them against macrophages.

Baumgartner showed that in the root canal there are gr+ facultative and as we get close to apex they turn to gr- anaerobic.

BPB (Black Pigmented Bacteroides) are gr- strictly anaerobic rod. Shah and Collins classified them to prevotella (break the sugar, saccharolytic) and Porphyromonas (Asaccharolytic) are the most common in abscess (gr- strict anerobic rod). Found to be associated with necrotic symptomatic teeth (Baumgartner (1989): 73% of canals containing BPB had abscesses or pus. Divided into Porphyromonas (asaccharolytic BPB): P. asacharolyticus, P. gingivalis, P. endodontalis. Divided into Prevotella (saccharolytic BPB): P. intermedia, P. nigrescens, P. melaninogenicus. P. denticola. P. loesscheii

The most common BPB isolated is **Prevotella nigrescens** (Baumgartner 1999).

Baumgartner & Faullker (1991): 84% of 90 PA lesions had IgG reactive to **P. intermedia**

Prev. melano is associated with pain (**Sundqvist 1989**).

Markus Haapasalo 1994: At least some bacteria are site specific. **P.intermedia** is associated with perio pockets whereas **P.nigrescens** associated with root canals. He also found that **p.gingivalis and P.Endodontalis are just found in the symptomatic apical periodontitis.**

Sundqvist 1994: Fusobacterium (gr- anaerobica) , Bacteroides, Peptostrep: Correlated highest with PA destruction. He also stated that bacterial strains can cause clinical symptoms. **Painful lesions have over 6 species of bacteria while painless lesions have 5 or less.**

Baumgartner: Demonstrates the presence of predominantly anaerobic bacteria in the apical 5 mm of infected root canals in teeth with carious pulpal exposures and periapical lesions. Number of obligate anaerobia bacteria increased with time and the apical portion.

Chavez: anaerobic bacteria can be identified using PCR. The walls of the necrotic root canals become colonized by a specialized mixed anaerobic biofilm. Also **F. nucleatum** recovered most frequently from the **acute dental abscess.**

Siqueira confirmed the presence of fungus in the canal. **Candida albicans** is by far the fungal species most commonly isolated from infected root canals, and this species has been considered a dentinophilic microorganism because of its invasive affinity to dentin. C albicans has also been discovered to be resistant to some intracanal medicaments, such as calcium hydroxide. Its ability to invade dentinal tubules and resistance to commonly used intracanal medicaments may help to explain why C albicans has been associated with cases of **persistent root canal infections.** This finding was also confirmed by **Haapasalo**.

Gomes (2015, JOE) Showed that the high incidence of Treponema species in RC and AAA samples from the same tooth indicated that they are important pathogens in acute endodontic infections. Their findings suggested that Treponema species are important pathogens involved in endodontic infections, particularly in cases of primary and acute infections.

Sabeti investigated the presence of Herpes virus in periapical region. The important finding of this study was that most teeth with necrotic pulp and periapical lesions harbored herpesviruses in periapical granulomatous tissue. **Herpesvirus and EBV** species in cooperation with endodontopathic bacteria may play major roles in the etiopathogenesis of **aggressive types of periapical pathosis in humans.**

Siqueira (2011, JOE) stated that **HHV-8** was for the first time detected and in a high prevalence. Papillomavirus and other herpesviruses were also found for the first time in endodontic abscesses. Although these findings suggest an association, **the specific role of viruses in the pathogenesis of acute apical abscesses awaits further clarification.**

The findings of HCMV (human cytomegalovirus) and EBV transcripts in apical periodontitis are controversial among the studies. **In a recent meta analysis Jakovljevic (2014, JOE)** stated that Herpesviruses are common in symptomatic and large-size periapical lesions, but such results failed to reach statistical significance.

Love study in regional variation in root dentinal tubeless infection: The pattern of bacterial infection of the cervical and mid root areas was similar, characterized as a heavy infection with bacteria penetrating as deep as 200 microns. Invasion of the apical dentin was significantly different, with a mild infection and maximum penetration of 60 microns. Therefore, **Yared & Bou Dagher** 1994 advocate apical preparation to 0.3-0.5 mm larger than original size. Also it is good to keep in mind the **Hapasalo study (2010, JOE)** regarding the penetration of NaoCl. Depth of penetration increased with increasing hypochlorite concentration, but the differences were small. Within each time group, depth of penetration with 1% NaoCl was about 50%–80% of the values with the 6% solution. Temperature, time, and concentration all contribute to the penetration of sodium hypochlorite into dentinal tubules.

Orstavik talked about dentinal tubules E. faecalis & Strep sanguis grew 300-400um into slabs of bovine dentinal tublues after 14-21 days. Presence of a smear layer delayed, but did not prevent, antimicrobial effects of medications.

Shovelton (1964) claimed that the larger the periapical lesion, the farther bacteria extend inside the dentinal tubules.

Enterococcus faecalis: gr+ facultative anaerobic diplococcic

Several studies have compared the frequency of E. faecalis detected in persistent and primary intraradicular infections. Some of them showed that E. faecalis is more often associated with failed endodontic treatments than primary infections (**Gomes JOE 2004; Siqueira JOE 2004**); whereas others indicate that no statistical difference was found between. Finally, **Zhang (Systematic review-2015)** reported that E. faecalis is more highly correlated with persistent intraradicular infections compared with untreated chronic periapical periodontitis.

Gomes, Molander: The microbial flora in canals after failure of RCT was limited to small number of diplococcic facultative anaerobic compared to polymicrobial nature of primary RTC composed of gr – obligate.

Stuart (JOE, 2006) reviewed the survival and virulence factors of E.faecalis:

- Endures prolonged periods of nutritional deprivation (**Sundqvist**)
- Binds to dentin and proficiently invades dentinal tubules (Love)
- Alters host responses
- Suppresses the action of lymphocytes
- Possesses lytic enzymes, cytolysin, aggregation substance, pheromones, and lipoteichoic acid
- Utilizes serum as a nutritional source
- Resists intracanal medicaments (i.e. $Ca(OH)_2$)
    - Maintains pH homeostasis
    - Properties of dentin lessen the effect of calcium hydroxide
- Competes with other cells
- Forms a biofilm

Tian (JOE 2013) stated that **LTA of E. faecalis** could inhibit the proliferation and induce apoptosis of human osteoblast-like MG63 cells.

Chavez (IEJ,2015): Different strains of E. faecalis can interact synergistically or antagonistically with a consortium of root canal bacteria. A possible mechanism underlying this, as well as potential differences in virulence, is production of different levels of proteases, which can cause detachment of neighboring bacteria and tissue damage.

E. faecalis strains from saliva and infected root canals have the potential to recruit PMNs in the infectious sites leading to inflammation via up-regulation of PMN IL-1α, TNF-α, MMP-8, and COX-2. PMNs can play an important role in killing of E. faecalis as shown by **Haapasalo (2011, JOE).**

Classic review of E.faecalis:

Molander (1998): Found Enterococcus faecalis in 78% of 100 failed NSRCT cases.

Siren (1997 IEJ): Found Enterococcus faecalis in 60% of failing NSRCT cases (cases tx by genl dentists in Finland).

Fabricius (1982): Unlike most endo infections, Ef can survive in RC system as single organism (rather than polymicrobial community). Confirmed in germ -free mice (Sobrinho (1998)).

Bystrom (1985): Importantly, E. faecalis is resistant to Ca(OH)2 tx. Confirmed by Reit & Dahlen (1988).

Estrella (1999 JOE): Ca(OH)2 demonstrated NO antimicrobial effect at 2, 3, & 7 days against E. faecalis, S. aureus in infected dentinal tubules (suggests antimicrobial effectiveness is due to concentration of [OH] and time of exposure).

.Distel (2002, JOE): E. Faecalis can form biofilm and become resistant to CaOH

Fuss (1997 IEJ): In vitro study: Roths > CRCS or Salapex at killing E.f in 24hr old mixtures; sealapex active at 7days after mix.

D'Arcangelo (1999): 0.5% = 1% = 2.5% = 5% NaOCl for antimicrobial effectiveness (11 strains inc E. faecalis; in fac aerobes -anerobes, microaerophiles, obligate anerobes). IMPORTANT POINT: Best when use at least 10 min contact time.

Heline (1998 IEJ): Chlorhexidine is effective in dentin infected with E. faecalis (ie chlorhex = NaOCl). Can survive prolonged starvation (Figdor)

Bacteiral flora in acute PA abscess: It is polymacrobial. **Siqueira and Siqueira** showed that 1) B. Forsythus 2) p.gingivalis 3) p.intermedia are the most common in Apical Abscess.

Qiu-Bo Yang (JOE, 2010): Bacterial DNA was present in all of the 11 purulence samples (apical abscess). The microflora of clinical purulence samples were profiled by the PCR-DGGE method, and overall 17 bacterial genera were identified. The number of bacterial phylotypes in the purulence samples ranged from 1–8. **Prevotella (24%), Fusobacterium (17.7%), Porphyromonas (13.9%), Lactobacillus (11.3%), Peptostreptococcus (8.3%), Streptococcus (6.4%), Eubacterium (3.8%), Campylobacter (3.3%), Trepone ma (2.6%), and Bulleidia (2.6%) were the most dominant genera found.**

Siqueira JR & F. barnett described the effect of LPS in postop pain. They suggest a positive correlation between bactaira LPS and Post OP pain. The same finding was also highlighted in **Schein & Schilder (1975)** found positive correlation between endotoxin levels and necrotic, painful teeth with PARLs.

Gomes (2012, JOE) conducted a study to compare the levels of endotoxins (lipopolysaccharides [LPSs]) found in primary and secondary endodontic infections with apical periodontitis by correlating LPS contents with clinical/radiographic findings. They found that the median value of endotoxins found in the presence of clinical symptoms was significantly higher than in asymptomatic teeth with primary infections. A positive correlation was found between endotoxin contents and a larger size of the radiolucent area (>3 mm). Also Teeth with primary endodontic infections had higher contents of endotoxins and a more complex gram-negative bacterial community than teeth with secondary infections.

Detection of **HIV** in the dental pulp of a patient with AIDS. **Glick M, Trope M**.

L. C. N. de Brito (IEJ, 2015): Immunological profile of periapical endodontic infections from HIV− and HIV+ patients. Findings suggest that after reducing the root canal bacterial load in HIV− individuals an anti-inflammatory response is generated whilst in + patients a pro-inflammatory response is sustained in the periapical area **(Outcome studies found no correlation with HIV statues but immunological studies found).**

Weston-Price: First talked about the **focal infection**. The historical background of the connection between dental infection and systemic diseases is related to the theory of 'focal infection', which was described as 'a localized or generalized infection caused by bacteria travelling through the bloodstream from a distant focus of infection **(Rosenhow 1909**). In the years following the description of this theory, numerous reports on the healing of systemic diseases following dental extractions and tonsillectomies were published, and in 1910, Dr. William Hunter called tooth restoration 'a veritable mausoleum of gold over a mass of sepsis.' (Hunter 1918). As a consequence of this theory, physicians started to advocate the removal of teeth with necrotic pulps as an alternative to or in conjunction with the removal of adenoids and tonsils to treat many diseases. Consequently, in the early twentieth century, endodontic treatment (ET) lost its importance within dental education as well as in the practice of dentistry (Grossman 1976).

Describe the Zones of Fish 1939. ICIS!!!!!!!

1) Necrosis / Infection – bacteria, PMNs
2) Contamination – bacterial toxins, lymphocytes, macrophages
3) Irritation – osteoclasts, lymphocytes, macrophages, granulomatosis
4) Stimulation – osteoblasts, fibroblasts
5) Conclusion - Cotton wool + bugs implanted into guinea pig mandibles 4-40 days. Infection remained
6) localized regardless of the duration or virulence of the organism. Rejected the Focal infection theory.

Are bacteria present in perapical lesions?

Yes: Tronstad anaerobic bacteria are able to survive and maintain in periradicular tissues. This finding was criticized by **Nair** who said their findings is due to contamination of samples.

NO: Walton and Nair said bacteria are not present in the periapical region. Inflammatory lesions seemed to resis the spread of bacteria, confining them to the canal.

Nair suggested that bacteria are present in the PA in the following situations: 1) Abscess 2) infected radicular cyst.

Baumgartner reported that incidence of bacteremia following RCT is very low 3.3 % regardless of pulpal statues and if you confine the RCT to root canal it can be prevented. **Siqueira** suggested that endo can cause bacteremia but there is no clear evidence that this bacteremia can initiate infection or disease in far sites.

"A **biofilm** is any group of microorganisms in which cells stick to each other on a surface. These adherent cells are frequently embedded within a self-produced matrix of extracellular polymeric substance (EPS). Biofilm extracellular polymeric substance, which is also referred to as slime (although not everything described as slime is a biofilm), is a polymeric conglomeration generally composed of extracellular DNA, proteins, and polysaccharides. Biofilms may form on living or non-living surfaces and can be prevalent in natural, industrial and hospital settings. The microbial cells growing in a biofilm are physiologically distinct from planktonic cells of the same organism, which, by contrast, are single-cells that may float or swim in a liquid medium"
(Stoodley; Lewis)

Biofilm bacteria are also intrinsically less susceptible to antimicrobial substances due to their slow rate of growth and adoption of a distinct biofilm phenotype, which differs from that of their planktonic counterparts **(Costerton et al. 1999).**

Bergenholtz (Endo topics): A biofilm makes root canal debridement more challenging because it is more resistant to antimicrobial agents than bacteria in planktonic form. Moreover, the matrix is a physical barrier against disinfecting agents.

Endo-Perio lesion:

Occasionally, the sinus tract will dissect through the periodontal ligament and drain through a gingival pocket, again simulating the clinical appearance of advanced periodontal disease of sulcular origin. **Simring and Goldberg** described this process as "**retrograde periodontitis**." They contrasted this to "marginal periodontitis" which progresses from the sulcus apically.

Chronic periodontal and endodontic inflammatory processes have three important similarities (Segura-Egea et al. 2012):
1. Both are chronic infections of the oral cavity;
2. Both are polymicrobial infections sharing a common microbiota with a predominance of Gram negative anaerobic bacteria **(Siqueira 2014).**
3. Elevated cytokine levels may be released systemically from acute and chronic manifestations of both disease processes, for example increased concentrations of inflammatory mediators have been detected both in the gingival crevicular fluid of subjects with PD and in the periapical tissues of endodontically involved teeth **(Caplan 2004, Caplan et al. 2006).**

What are common **perio pathogens**?
Red complex Bacteria: P. gingivalis, T. forsythensis & T. denticola
Other bacteria linked to perio disease: Actinobacillus actinomycetemcomitans, B. forsythus & P. intermedia.
Trope – spirochetes common in perio abscesses but less likely in endo abscesses

Janssen: Relation between Periodontal pocket bacteria and root canal bacteria. Root-canal infection, evident as a periapical radiolucency, if left untreated may in the long term perspective result in retarded or impaired periodontal healing following periodontal therapy. Healing after scaling and root planing was also significantly impaired over time by the presence of a root canal infection.

Can Endo pathosis create perio pathology? Sinai & Soltanoff – rat study showed pulpal disease affects the periodontium quickly with inflammation; perio disease affects the pulp slowly with degenerative changes

Does perio disease cause endo pathosis?
Yes: **Seltzer**: disease caused through lateral/accessory canals and vice-versa
Langeland, Rodregues & Dowden – if all main apical foramina are involved
Kipioti & Kobayashi (2 sep. studies) – caries free teeth with endo path showed similar microorganisms in perio pockets and root canals
No: **Mazur & Massler / Czarneck & Schilder**: Histo studies showed no correlation

Who **discussed endo-perio terminology**?
Simon (1972) – Primary endo; Primary endo with 2nd perio; Primary perio; Primary perio wth 2nd endo; true combined lesions (ie root fx)

Does perio tx affect the pulp?
Wong & Hirsch: pulpitis was noted adjacent to areas of root planning/scaling

Does endo tx affect future perio tx?
Dunlap: in vitro study found RCT does not interfere with growth of fibroblasts on planed dentin surfaces.

*What is the biologic width? Combined width of connective tissue and epithelial attachment above the crestal bone

Gargiulo, Wentz & Orban – sulcus depth(0.7mm)+ epithelial attachment (1mm)+ CT attachment (1.1mm)= **2.04mm**

Euiseong Kim 2008 JOE (Korea): Endodontic microsurgery done on regular CAP cases and on Endo-Perio cases. 263 teeth with 2 year follow up. When buccal bone was lost, Calcium sulfate was used with CollaTape cover. **Pure endo had 95.2% success. Endo Perio had 77.5% success. It might be concluded that the combined Endo-Perio lesions can jeopardize the outcome of the RCT.**

Setzer F et al 2011 (JOE): Molar endodontic treatments with crown placement. Information recorded was: crown lengthening, periodontal diagnosis, attachment loss, furcation involvement, mobility, internal resorption, external resorption, periradicular resorption. 4-year minimum follow-up. The only preoperative factors significant for the prognosis of restored endodontically treated molars (Among the mentioned factors) were related to periodontal prognostic value and attachment loss.

Gupta (JOE, 2015) in a prospective randomized clinical trial evaluated the effect of a time lapse between endodontic treatment and nonsurgical periodontal treatment on periodontal healing of concurrent endodontic-periodontal lesions without communication. It was found that **nonsurgical periodontal treatment may be performed simultaneously with endodontic treatment in the management of concurrent endodontic-periodontal lesions without communication, and an observation period after endodontic treatment may not be required.**

Post and Post space preparation:

Ferrule: band of tooth structure around the tooth which is 1.5-2mm

Juloski (2012, JOE) published a guideline regarding the **ferrule effect**: "The presence of a 1.5- to 2-mm ferrule has a positive effect on fracture resistance of endodontically treated teeth. If the clinical situation does not permit a circumferential ferrule, an incomplete ferrule is considered a better option than a complete lack of ferrule. Including a ferrule in preparation design could lead to more favorable fracture patters. Providing an adequate ferrule lowers the impact of the post and core system, luting agents, and the final restoration on tooth performance. In teeth with no coronal structure, in order to provide a ferrule, orthodontic extrusion should be considered rather than surgical crown lengthening. If neither of the alternative methods for providing a ferrule can be performed, available evidence suggests that a poor clinical outcome is very likely".

Sorenson and also Goerig talked about criteria of an acceptable post and restoration of endodontically treated tooth: **4SPAF: 4 mm, Serrated, Parallel, as long, Ferrule.** Acceptable Posts should have following criteria: 1/3 MD with of root, 4mm of GP left, half in to the bone, it should be in widest and straightest canal, it must be 2/3 of the root or equal to clinical crown.

According to **Sorenson** while crowns significantly improved the success of endodontically treated posterior teeth, they did not do so for anterior teeth.

Trope in 1985 argued that post space preparation weakens the tooth and post do not strengthen the tooth structure. Based on this findings **Sorenson** suggested that since a post does not strengthen an RCT tooth and the preparation of a post space may increase the risk of root fracture and treatment failure**, the decision whether to use a post in any clinical situation must be made judiciously.**

Kane JJ, Burgess JO. Modification of the resistance form of amalgam coronal-radicular restorations. J Prosthet Dent 1991;65: 470-4. Many ET molars do not require a post because they have more tooth substance and a larger pulp chamber to retain a core buildup

Cailleteau JG: A comparison of intracanal stresses in a post-restored tooth utilizing the finite element method. **J Endod 1992:** Results indicate that the stress patterns within the root are altered as a result of post insertion. Specifically, the maximum bending stresses are associated with the apical termination of the post, and **post placement does not result in a uniform distribution of stress along the canal wall**. Endodontically treated teeth with pulp and crown models (no post) demonstrated a gradual increase in stress levels to a maximum which occurred approximately 2 mm apical to the canal orifice. In contrast, the post-restored model demonstrated a decreased level of stress along the coronal facial portion of the root surface which peaked abruptly near the apical end of the post. This area of peak stresses within the post model appears to be the result of the maximum bending occurring at the apex of the post.

Haddix & Mattison (1990) Recommended remove GP with hot instrument for post space preparation. **GG burs** tend to "pull" GP and may **disrupt apical seal** which might affect the long term success of RCT.

Based on **Madison** findings leave at least 4mm GP when placing post.

Madison, Zakariasen showed that there is no difference if you prepare the post space at the time of obturation or later regarding the seal and micro leakage. However, **Karapanou et al 1996** showed that Post-space preparation can be undertaken immediately following obturation to avoid twisting gutta-percha and breaking the seal when sealer is set.

Kuttler said there might be a risk of perforation using gates for post space preparation. Dentin thickness correlates inversely to post space diameter. A no. 4 Gates-Glidden drill caused strip perforations in 7.3 percent of the canals studied, and therefore the **authors recommend that Gates-Glidden drills larger than a no. 3 not be used in these roots**. After endodontic treatment, the furcation-side dentin thickness was less than 1 mm in 82 percent of the teeth.

Hagge MS. Investigated the effect of three root canal sealers on the retentive strength of endodontic posts luted with a resin cement. **Int Endod J 2002**. Eugenol containing sealer, AH-26, and Sealapex did not affect the retention of endodontic posts luted with Panavia cement; therefore, eugenol avoidance is unnecessary when selecting sealers.

Schwartz RS. Effects of eugenol and noneugenol endodontic sealer cements on post retention. J Endod 1998. The type of sealer (Roth's or AH-26) had no effect on post retention with either cement (ZnPO4 or Panavia). Post retention was significantly greater with the zinc phosphate cement than the resin cement.

AL-Omiri (2010, JOE) reviewed the fracture resistance of tooth restored with posts. It was suggested that fracture resistance was improved if tooth structure loss was limited, a ferrule was obtained, a post with similar physical properties to natural dentine was used, and adhesive techniques for post luting and coronal restoration were used. Adhesively luted resin/fiber posts with composite cores appear to be the best currently available option in terms of tooth fracture and biomechanical behavior.

Fokkinga et al (IEJ, 2005) reported that the presence or absence of metal/fiber posts did not affect the fracture resistance and failure modes of endodontically treated **premolar** teeth with resin composite crowns and no retained coronal tooth structure. Therefore, they suggested that **posts are not necessary for the restoration of such teeth**. Also, **Mohammadi et al (JOE, 2009)** found no difference in fracture resistance of premolars restored with direct resin composite in the presence or absence of fiber post and cusp coverage.

In a meta analysis (2013, JOE) Zhou compared the fracture resistance between cast posts and fiber posts. It was mentioned that **cast posts had higher fracture resistance than fiber posts.**

Flare-up:

An endodontic flare-up is defined as an acute exacerbation of a periradicular pathosis after the initiation or continuation of nonsurgical root canal treatment.

Seltzer & Naidrof (1985 JOE) investigated the immunology of flare ups and factors related to flare-up mechanism:
C: Chemical mediators
C: Cyclic nucleotides
L: Local adaptaion theory
I: Immune response
M: Microbial factors
P: Psychological
P: Pressure

Review of microbial cause of Endodontics Flare-ups (Siqueira, 2003; Following Figures are reprinted from Siqueira study):

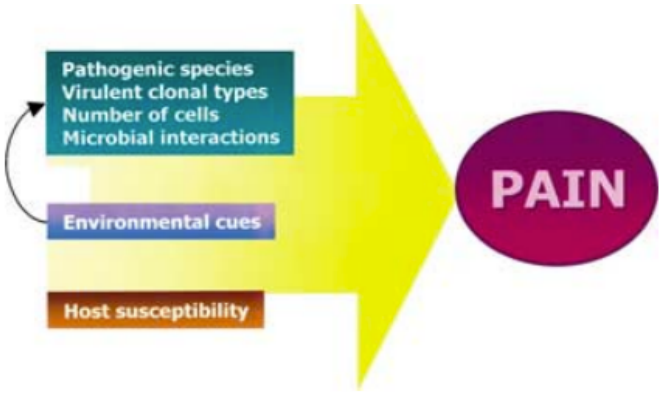


Figure 1 Factors influencing the development of pain associated with endodontic infections. In addition to the pathogenic species, other microbial and host-related factors are also highly likely to be involved in the pathogenesis of symptomatic periradicular diseases (see text for more discussion).

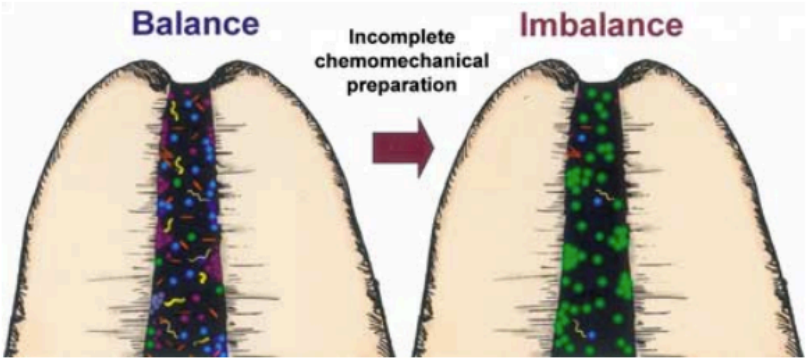


Figure 4 Incomplete chemo-mechanical preparation induces changes within the root canal system that may favour the overgrowth of certain species. If overgrown bacteria reach sufficient number and express virulence genes, they can induce damage to the periradicular tissues, and a flare-up may ensue.

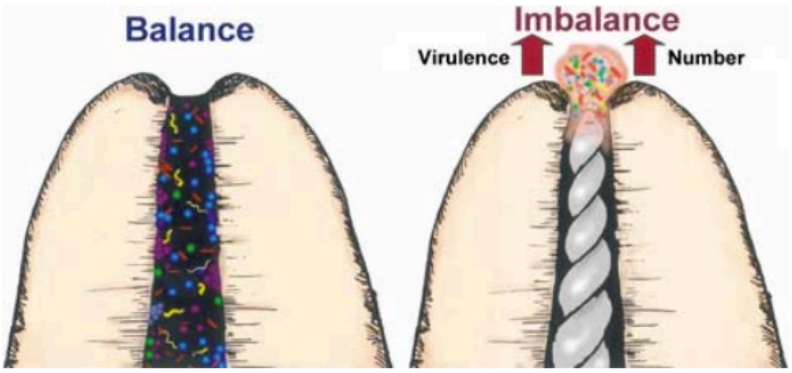


Figure 2 Apical extrusion of microorganisms and/or their products during chemo-mechanical procedures may induce acute periradicular inflammation to re-establish the balance between aggression and defence. Such response depends on both the number and virulence of extruded microorganisms.

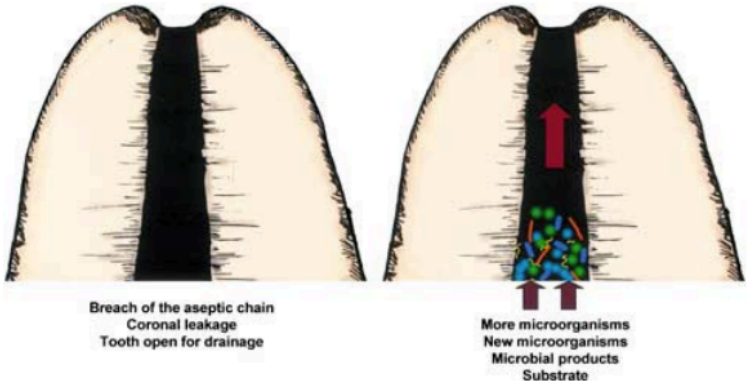


Figure 5 New microbial species, more microbial cells and substrate from saliva can be carried into the root canal system during treatment, between appointments or following treatment. If a secondary infection establishes itself, a flare-up may occur.

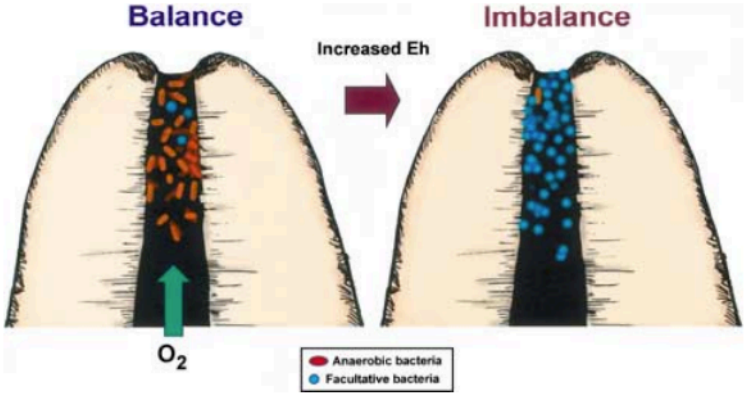


Figure 6 Entrance of oxygen into the root canal during treatment may favour the overgrowth of facultative bacteria that resisted chemo-mechanical procedures. This mechanism is only conjectural, and there is no clear evidence substantiating this theory.

Ana Arias (JOE, 2012): Predictive models of pain following root canal treatment: a prospective clinical study: Both the internal and external validity of the models were assessed. The internal validity was tested in two steps: assessing calibration and discrimination. Calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. **This test evaluates whether the rates of the observed event match the expected event rates in subgroups of the model population** (Hosmer & Lemeshow 2000). Small P-values indicate a lack of fit of the model.

k[a]	Variable (test/reference category)	Coefficient	Odds ratio (95% CI)	*P*-value
−0.8537	Periapical radiolucencies (yes/no)	−0.94	0.4 (0.2, 0.7)	0.003
	Previous pain (yes/no)	0.71	2 (1.2, 3.3)	0.006
	Group of teeth (nonmolar/molar)	−0.77	0.5 (0.3, 0.8)	0.003
	Previous emergency access (yes/no)	0.59	1.8 (1, 3.2)	<0.05
	Occlusal contact (yes/no)	1.17	3.3 (1.9, 5.6)	<0.0001

The predictive models showed that the incidence of post endodontic pain was significantly **lower** when the treated tooth was **not a molar**, **demonstrated periapical radiolucencies** (p=0.003), there was **no history of previous pain** (p=0.006) or emergency endodontic treatment (p=0.045) and there was **no occlusal contact (p<0.0001). It was also demonstrated that the presence of a occlusal contact is a strong predictor!!**

Harrington & Natkin (1992 DCNA) suggested that necrotic teeth are more likely to have flare-ups; especially if debris is extruded. This finding was also confirmed later by **Siqueira (2005). Please remember** Crown-down (**Ruiz-Hubbard & Gutmann** 1987 JOE) and balanced-force (McKendry 1990 JOE) extruded less debris than step-back instrumentation.

Torabinejad, Ung and Kettering analyzed factors that are associated with flare-ups: Chronic apical abscess has 0% flare up (Just make sure the sinus tract is open!!). Endodontic flare-ups seem to be more prevalent among **females** under the age of **20 years**, and may occur more in **maxillary lateral incisors**; **mandibular first molars due to missed canals**, when there are **large periapical lesions**; and in the **re-treatment** of previous root canals. The presence of **pre-treatment pain** may also be a predictor of potential post-treatment flare-ups. **Presence of systemic diseases, use of intracanal medications, and penetration of the foramen with small instruments during length determination had no significant effect on the frequency of these emergencies.**

Based on Walton & Fouad (1992) study **best predictors of post op pain are pre-op pain or swelling**. Also Walton released that antibiotics are not effective than analgesics in reducing inter-appointment flare-up. **So we do not prescribe antibiotics to reduce the flare-up rates or post-op pains.**

In **Tsesis et al Meta analysis** the frequency of flare-ups was estimated 8.4%.

Reasons for flare-ups can be summarized in the following studies:
1) Harrington GW, Natkin
2) Seltzer: Endodontic flare-ups may occur because of a variety of reasons, including **preparation beyond the apical terminus**, **over-instrumentation**, **pushing dentinal and pulpal debris** into the periapical area, **incomplete removal of pulp tissue**, **overextension of root canal filling material, chemical irritants** (such as irrigants, intracanal medicaments, and sealers), **hyper-occlusion**, **root fractures**, and **microbiologic** factors.

Torabinejad & Kettering: Females 40 - 59, Mandibular premolars, Presence of allergies, preop pain, little or no PARL, no medications (painkillers), retreatments, no sinus tract can be considered as the factors that increase the chance of flare ups.

Walton reported the total incidence of flare ups **17-18% if we have pre op pain and swelling**, **6.5% in necrotic cases, 1.3% in vital cases, 0% in case of sinus tract. ** Overall incidence is 3.6%**

Elizabeth Applebaum, Asma Khan (2015-JOE) confirmed that **genetic variants in COX-2** associated with **post-treatment pain** after endodontic treatment.

Torabinejad suggested that with multirooted teeth, a pulpotomy (removal of the coronal pulp or tissue from the widest canal) has been advocated for emergency treatment of irreversible pulpitis. **This can be considered a clinical success which can lead to late failure if we do not remove the causative agents.**

Rosenberg, Babick, Schertzer and Leung (JOE)1998: 4 criteria to adjust occlusion: Occlusal reduction should prevent postoperative pain in those patients whose teeth initially exhibit **pulp vitality**, **percussion sensitivity**, **preoperative pain, and/or the absence of a periradicular radiolucency**. WHICH RINGS THE BELL FOR **SIP/SAP diagnosis**. This finding was also confirmed by **Cunningham**. However, **Masoud Parirokh (2013, JOE)** stated that Occlusal surface reduction did not provide any further reduction in postoperative pain for teeth with **irreversible pulpitis and mild tenderness to percussion** compared with no occlusal reduction (But consider in this study they did not obturate the root canals in the first visit!!)

Creech & Walton (1984 JADA): Adjust occlusion only as **needed**; prophylactic adjustment does not reduce pain.

Gatewood RS, Himel VT, Dorn S: In vital teeth in which the inflammation has extended periapically, which will present with pretreatment pain to percussion, **occlusal reduction has been reported to reduce posttreatment Pain.**

Keenan JV, Farman AG, Fedorowica Z, Newton JT: In a Cochrane Systematic Review supported the Walton findings and reported that there is no evidence to support the use of antibiotics for pain relief in irreversible pulpitis. This finding was also confirmed by **Reader** who showed that Pen VK did not decrease flare-ups with IP. Amox did not help decrease flare-ups with necrotic, asymptomatic teeth. Pen VK did not decrease flare-ups with necrotic, symptomatic teeth.

Walton and Torabinejad (2002) reported that in **intra-appointment flare-ups** with necrotic pulp and no clinical swelling there might be an **acute apical abscess which is confined to bone and not show a swelling**. In this cases, patency (apical trephination) reduce the pressure and pain significantly.

Kerekes & Tronstad (1979): (Root canal done by undergraduate, hand file and lateral condensation): **No change in prognosis for success if case has flare-up (opposed to Ng study)**. Roots without periradicular radiolucency prior to treatment showed better success rate than those with radiolucency. No difference in success between vital and necrotic pulps, or in teeth with flare-ups during tx. Adequate seal and the apical level of the root filling were significant factors for the success of tx.

Walton (1977) compared the effect of three intracanal medicaments (Formocresol, Ledermix, and calcium hydroxide) on the incidence of post-instrumentation flare-ups**. 2.5%** flare ups were seen. No significant difference was found in the flare-up rate among the three intracanal medicaments.

Ehrmann EH: The relationship of intracanal medicaments to postoperative pain in endodontics: Painful teeth with acute apical periodontitis that had been dressed with Ledermix paste gave rise to less pain than that experienced by patients who had a dressing of calcium hydroxide or no dressing at all. It was suggested that **Ledermix is an effective intracanal medicament for the control of postoperative pain associated with acute apical periodontitis, with a rapid onset of pain reduction.**

J.J. Segura-Egea, R. Cisneros-Cabello: Pain associated with root canal treatment **Int Endod J (2009)**: There are no significant differences in relation to gender or age groups. Mandibular teeth had a significantly ($P < 0.05$) higher percentage incidence of pain in comparison with maxillary teeth. Pain was absent in 63% of anterior teeth compared with 44% in posterior ones ($P < 0.01$). Interventions shorter than 45 min resulted in a significantly higher percentage of pain absence ($P < 0.05$). **Root canal treatment was significantly ($P < 0.05$) more painful in teeth with irreversible pulpitis and acute apical periodontitis compared to the group with necrotic pulps and chronic apical periodontitis ($P = 0.049$).**

Harrington GW, Natkin E: Midtreatment flare-ups: The principal modality for **managing swelling secondary to endodontic infections** is to achieve drainage and remove the source of the infection.

Bence & Meyers '80; Simon '82; Seltzer & Naidorf '84: leaving teeth open between appointments is not recommended due to bacterial recontamination, food debris, blockage of canals and higher chance flare-ups. **Also Weine (1975 OOO)** showed that teeth left closed had fewer exacerbations.

Haapasalo (1997, IEJ): If root canal had been unsealed at some point between treatments, enteric bacteria were found more frequently. This indicate the importance of good seal between different appointment. Also the higher the number of appointments the rate of enteric bacteria would be higher.

Medication, Anesthesia and pain control:

K. Hargreaves= principle of pain control is 3D⇒Diagnosis, Definite dental treatment, Drugs

Cohen: lip anesthesia is not a reliable indicator of pulpal anesthesia. The use of DDM is a reliable method of determining true pulpal anesthesia.

Marshal systematic review regarding the effect of steroids in post-op endo pain (From Dr. Krell's study guide):

Effects of glucocorticoids on inflammation:

- Inhibit AA metabolites by inhibition of phospholipase A2
- Decreased transcription of inflammatory cytokines IL-1, 2, 3, 4, 5, 6, 11, 12, TNFa
- Decreased transcription of chemokines IL-8, RANTES
- Decreased iNOS
- Decreased COX2 transcription by monocytes/macrophages
- Decreased neurogenic inflammation by inhibiting tachykinins
- Decreased bradykinin due to increased ACE synthesis

Glucocorticoids may have widespread effects on many organ systems but these effects are typically only seen at supra-physiological doses given over a long-term period, usually more than 2weeks.

- Intraoral IM injection or an intraosseous injection is preferable over an extraoral IM injection. Intraoral injection of steroid is preferable as no assumption about patient compliance is required. A dose of 6–8mg of dexamethasone or 40mg of methylprednisolone appears from the literature to be appropriate.
- If an oral route is chosen 48mg methylprednisolone/day for 3days and by extrapolation 10–12mg dexamethasone/day for 3 days should provide significant post treatment pain relief.

Corticosteroids may be more efficacious in attenuating pain associated with pulpal necrosis and associated radiolucencies compared to pain associated with irreversible pulpitis since these conditions are associated with more complex chronic inflammatory processes.

The use of steroids have been investigated in different routs:

1) **Intracanal: Morse** showed reduced post op pain following intracanal use of dexa in vital cases.
2) **Systematic: Reader and Marshal** showed reduction in the post op pain following administration of oral or intaosseous. Reader showed that **intraosseous injection of Depo-Medrol** reported less pain and percussion pain while taking fewer pain medications. Clinically the intraosseous injection of Depo-Medrol could be used to temporarily alleviate the symptoms of irreversible pulpitis until definitive treatment can be rendered.
3) **PDL: Kaufman** showed reduced pain after PDL injection of steroidal **anti- inflammatory- slow-release methylprednisolone (Depomedrol).**

Jalalzadeh (JOE, 2010) investigated the effect of prednisolone premedication on post RCT pain. This study suggests that a preoperative, single oral dose of prednisolone substantially reduced postendodontic pain

Khaly Bane (JOE, 2016) assessed the effectiveness of intraosseous Methylprednisolone Injection **(A Reader)** for Acute Pulpitis Pain in comparison to conventional emergency pulpotomy **(Tronstad)** in a RCT study. It was shown that at day 7 the patients in the methylprednisolone group reported less intense spontaneous and percussion pain in the day 0–day 7 period than the patients in the pulpotomy group. Methylprednisolone treatment took approximately 7 minutes (4.6–9.3) less to accomplish than pulpotomy (or about half the time).

Maximum dosage of Acetaminophen =3 g in 24h. Acetaminophen is a safer drug in patients who have GI problems compared to NSAID. **Max ibuprofen dose =3200**

Cooper (flexible medication): For moderate to severe pain relief, ibuprofen, an NSAID, has been found to be superior to aspirin (650 mg) and acetaminophen (600 mg) with or without codeine (60 mg). Also, ibuprofen has fewer side effects than the combinations with opioid. The maximal dose of 3.2 g in a 24-hour period should not be exceeded. **Patients who take daily doses of aspirin for its cardioprotective benefit can take occasional doses of ibuprofen; however, it would be prudent to advise such patients to avoid regular doses of ibruprofen**. These patients would gain more relief by taking a selective cyclooxygenase (COX)-2 inhibitor, such as diclofenac or celecoxib.

Andre Mickel: It was found to be statistically significant that **600 mg ibuprofen given four times per day** was the preferred analgesic prescribed for patients regardless of their perceived level of pain, endodontic diagnosis, or treatment rendered. Narcotics were prescribed in the following conditions: postsurgical pain (28%), postoperative flare-up (31%), or severe pain associated with a necrotic pulp and acute periradicular abscess (34%)

Nixdorf and Law: meta-analysis on the **prevalence of persistent pain after endodontic therapy**: In conclusion, the frequency of all-cause tooth pain at 6 months or longer following root canal therapy of permanent teeth is **approximately 5%.** Higher persistent pain estimates (>7%) likely reflect a lower limit of chronic pain frequency after endodontic procedures *** Patients reporting "tooth" pain 6 months after RCT had a nonodontogenic pain diagnosis accounting for some of this pain, with temporomandibular disorder being the most frequent nonodontogenic diagnosis.

Kretzschmar (OOO, 2003): Sinusitis should be considered in differential diagnosis of pain in **post maxillary** tooth.

Haas DA. An update on local anesthetics in dentistry. J Can Dent Assoc 2002.
Review article.
1. Biotransformation of amide LA occurs in the liver. Reduced hepatic fxn does not increase duration of anesthesia but predisposes to toxic effects. Use reduced dosages. Ester local anesthetics undergo extensive hydrolysis in the plasma by pseudocholinesterase enzymes
2. Methemoglobinemia is associated with articaine and benzocaine
3. Articaine and prilocaine are associated with increased parasthesia.
4. Malignant hyperthermia occurs with exposures to inhalation anesthetics, not local anesthetics.
5. Lido and prilocaine are preg category B; others are C
6. 7mg/kg is max lido dose. (4.4mg/kg is Malamed/conservative)

Moore PA. Adverse drug reactions to local anesthesia. Dent Clin North Am 2002.
Local anesthesia toxicity: Initial symptoms include tremors, muscle twitching, and convulsions. Respiratory depression, lethargy, and LOC may follow. Cardiovascular depression and hypoxia secondary to respiratory depression can rapidly produce serious outcomes including cardiovascular collapse, brain damage, and death.
Methemoglobinemia: caused by metabolites of prilocaine, with symptoms occurring 1-3 hrs after treatment. Cyanosis without respiratory distress may be apparent when met-Hgb levels reach 10-20%. Vomiting and headache have been described, as has dyspnea, seizures, stupor, coma, and death at levels higher than 20%.

** is a disorder characterized by the presence of a higher than normal level of methemoglobin (metHb, i.e., ferric [Fe3+] rather than ferrous [Fe2+] haemoglobin) in the blood. Methemoglobin is a form of hemoglobin that contains ferric [Fe3+] iron and has a decreased ability to bind oxygen.

What is methemoglobinemia?

Wilburn-Goo D, Lloyd LM. When patients become cyanotic: acquired methemoglobinemia. J Am Dent Assoc 1999. Methemoglobin normally is present in the blood at levels <1%. Levels may become toxic as hemoglobin is oxidized to methemoglobin after local anesthetics such as benzocaine and prilocaine are administered. Overdoses occurring in dental practice are rare, accounting for 9 of 100 overdoses. Such cases have prompted maximum recommended dose changes for prilocaine (4mg/lb max). Benzocaine doses of 15-20mg/kg may cause methemoglobinemia, and a 1 second spray of 20% topical benzocaine delivers 60mg. Symptoms may develop hours after administration. Patients at increased risk include those with heart disease, anemia, G6PD deficiency, children<2, and elderly.

What are some reasons for local anesthetic failure?

Roy ML, Narahashi T. Differential properties of tetrodotoxin-sensitive and tetrodotoxin-resistant sodium channels in rat dorsal root ganglion neurons. J Neurosci 1992.
TTX-R sodium channels are resistant to local anesthesia.

Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: mechanisms and management. Endodontic Topics 2002.
Mechanisms of action: recent studies show that local anesthetics preferentially block myelinated fibers over unmyelinated.
Reasons for anesthesia failure:

1. Anatomical- accessory innervation
2. Tachyphylaxis- reduced responsiveness of receptors to drug (does not occur)
3. Tissue pH- uncharged base crosses membrane; charged acid blocks Na channel. Low pH causes LA to be trapped in the charged acid form that can't cross membranes. **Mepivacaine is more resistant to ion trapping due to it's lower pKa** (7.6 vs 7.9 for lidocaine). Problem with this theory: pH change is restricted to area of abscess.
4. Inflammation effect on blood flow- vasodilation carries away LA faster; may occur with infiltration.
5. Inflammation affects nociceptors by activation and sensitization- Bradykinin activates unmyelinated C fibers. PGE2 causes sensitization, reducing the threshold for firing, so that gentle stimuli (heartbeat) can now activate a neuron. Nerves sprout and grow into areas of inflammation, increasing the size of their receptive field. Inflammation causes increased neuropeptides (SP, CGRP). TTX-resistant Na channels are more resistant to lidocaine. TTX-R Na channel activity doubles after exposed to PGE2!
6. *Central Sensitization*- increased excitability of central neurons due to a barrage of nociceptive impulses. Causes an exaggerated CNS response to even gentle peripheral stimuli.
7. Psychological factors- apprehension causes reduced pain threshold.

Approaches for managing failures:

1. Supplemental LA: another block with 3% mepivacaine (due to low pKa) at a higher level (to increase nerve exposed and block mylohyoid), PDL, intraosseous, intrapulpal.
2. Adjunctive drugs: NSAID (reduced PGE2 decreases nociceptor sensitization and decreases TTX-R Na channel activity)

Christine M. Sedgley: Does Articaine Provide an Advantage over Lidocaine in Patients with Symptomatic Irreversible Pulpitis? A Systematic Review and Meta-analysis (JOE, 2015)

Within the maxillary infiltration, there was no significant difference between articaine and lidocaine. For combined mandibular anesthesia studies that used any delivery route, articaine was superior to lidocaine. Further subgroup analysis showed no difference when used for mandibular block anesthesia alone. However, when used for supplemental infiltration after (successful) mandibular block anesthesia, articaine was significantly more effective than lidocaine. **This systematic review of double-blind, randomized clinical**

trials provides level 1 evidence to support the use of articaine for patients with symptomatic irreversible pulpitis. There is a significant advantage to using articaine over lidocaine for supplementary infiltration after mandibular block anesthesia but no advantage when used for mandibular block anesthesia alone or for maxillary infiltration.

Corbett 2008 (JOE, Newcastle UK): 4% Articaine infiltrations (buccal + lingual) on lower first mandibular molars had similar EPT testing anesthesia as IANB (~60-70% rate of anesthesia). Subjective tooth numbness was more with IANB.

Remmers, Glickman et al 2008 (JOE, Dallas Texas): 30 teeth with irreversible pulpitis. Intra Flow intra-osseous injections had 87% success EPT 80/80. IAN block had 60% success EPT 80/80.

Stanley W et al 2012 JOE: Mandibular teeth with irreversible pulpitis had a statistically significant increase in the success of the IAN block when supplemented with 30-50% **nitrous oxide sedation.**

Aggarwal V et al 2012 JOE: Increasing the volume of 2% lidocaine to **3.6ml** improved the success rates as compared with 1.8ml. **54% success with 3.6ml VS 26% success with 1.8ml.**

Aggarwal (2012, JOE) in another study assessed the effect of injection rate on success of anesthesia. It was found that **Rate of injection has no effect on anesthetic success of IANB**, but slow injections were more comfortable than rapid injections.

Masoud Parirokh (2012, JOE) stated that **use of topical anesthesia had no significant effect on pain during either needle penetration or injection.** Pain during injection had no significant effect on the success of anesthesia.

In theory, using 3% mepivacaine initially for an inferior alveolar nerve (IAN) block would decrease the pain of injection, provide faster onset, and increase anesthetic success. **However Reader (JOE, 2014)** stated that the combination of 3% mepivacaine plus 2% lidocaine with 1:100,000 epinephrine was equivalent to the combination of 2 cartridges of 2% lidocaine with 1:100,000 epinephrine in terms of injection pain, onset time, and pulpal anesthetic success for the IAN block.

Al Reader (JOE, 2015): The incidence of missed blocks for asymptomatic subjects was 6.3% for the 1-cartridge volume and 3.8% for the 2-cartridge volume. For patients presenting with irreversible pulpitis, the incidence of missed blocks was 7.7% for the 1-cartridge volume and 2.3% for the 2-cartridge volume. In both asymptomatic subjects and patients with irreversible pulpitis, **the 2-cartridge volume was significantly better than the 1-cartridge volume.** Concerning missed IAN blocks, it can be concluded that **administration of a 2-cartridge volume was significantly better than a 1-cartridge volume in both asymptomatic subjects and emergency patients presenting with irreversible pulpitis.**

Few studies have evaluated the effectiveness of the Gow-Gates and Vazirani-Akinosi techniques in patients presenting with symptomatic irreversible pulpitis**. Reader stated that (JOE, 2015)** that for patients who achieved lip numbness neither the Gow-Gates technique nor the Vazirani-Akinosi technique provided adequate pulpal anesthesia for mandibular posterior teeth in patients presenting with symptomatic irreversible pulpitis. Both injections would require supplemental anesthesia.

Randomized double-blind clinical trial by Kanaa (JOE, 2012) showed that there was **no significant difference** in efficacy between 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:80,000 epinephrine in achieving anesthesia in maxillary teeth with irreversible pulpitis after buccal infiltration.

Kanna (JOE, 2012) also investigated the efficacy of different supplementary local anesthesia techniques following failure of initial IANB. It was concluded that **IANB injection alone does not always allow pain-free treatment for mandibular teeth with irreversible pulpitis. Supplementary buccal infiltration with 4% articaine with epinephrine and intraosseous injection with 2% lidocaine with epinephrine are more likely to allow pain-free treatment than intraligamentary and repeat IANB injections with 2% lidocaine with epinephrine** for patients experiencing irreversible pulpitis in mandibular permanent teeth.

Yared GM, An evaluation of 2% lidocaine with different concentrations of epinephrine for inferior alveolar nerve block. J Endod 1997. No statistically significant differences in success and failure were found among the 1:50,000, 1:80,000, and 1:100,000 concentrations of epinephrine

Rosenberg PA: Role of the anesthetic solution in intrapulpal anesthesia. J Endod 1975. **Intrapulpal administration produces anesthesia via pressure.**

Reader declared that a buccal infiltration of a cartridge of 4% articaine with 1:100,000 epinephrine will not provide profound pulpal anesthesia of the first molar. A solution to this problem is the addition of a buccal infiltration of 4% articaine with 1:100,000 epinephrine to an IAN block. Reported success rates of 88% by **Haase et al** and 92% by **Kanaa et** al have been shown.

In maxillary infiltration **Reader (2011, JOE**) showed the success rates were 88% for the buccal infiltration and **95% for the buccal plus palatal infiltration**. The difference was not statistically significant. The buccal plus palatal infiltration significantly increased the incidence of pulpal anesthesia from 21 minutes through 57 minutes. Although there was an increased incidence of pulpal anesthesia with the combination buccal plus palatal infiltration, anesthesia was not provided for 60 minutes.

Reader (JOE, 2010) showed that for the maxillary first molar, the 3.6 mL volume of the lidocaine formulation provided a statistically longer duration of pulpal anesthesia than the 1.8 mL volume.

Abazarpoor (JOE, 2015) stated that increasing the volume of articaine provided a significantly higher success rate of IANBs in mandibular first molar teeth with symptomatic irreversible pulpitis, but it did not result in 100% anesthetic success.

S.F. Malamed: Articaine hydrochloride: a study of the safety of a new amide local anesthetic J Am Dent Assoc, (2001): The chemical composition of articaine contains a unique thiophene ring instead of the benzene ring found in lidocaine and other amide local anesthetics. This difference increases lipid solubility, thereby increasing diffusion through the lipid membrane of the epineurium, which purportedly explains its faster onset and higher success rate when compared with lidocaine

A. Reader: Anesthetic efficacy of the periodontal ligament injection after an inferior alveolar nerve block JOE 1996: Concluded that **adding the PDL injection to an IAN block increased the incidence of pulpal anesthesia for the first 23 min in the first molar.**

Walton & Garnick (1982): PDL injection needs back pressure.

Walton (1981): Mandibular molars required supplementary anesthesia more frequently than other types of teeth. PDL injecting under strong backpressure was important; the greatest frequency of success was attained when injecting under pressure. Onset of anesthesia was generally **very rapid,** usually immediate. **The length**

and gauge of needle were unimportant in attaining anesthesia. The overall frequency of success in attaining anesthesia with this injection was 92%. This rate included situations in which the injection was administered more than once.

Kim said that PDL injection (vasoconstrictive) cuts down blocked blood supply to the pulp up to 60 mins. Vasoconstriction is mechanism of action.

Torabinejad M: PDL injection has no long-term deleterious effects on pulps of human premolars.

Reader A: 2% Lido with 1:100,000 epi is preferred for PDL and was more effective than anesthetics w/o epi. **Epi is important. Average pulpal anesth.=20min**.

V. Aggarwal: **Comparative evaluation of effect of preoperative oral medication of ibuprofen and ketorolac on anesthetic efficacy of inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis: a prospective, double-blind, randomized clinical trial** J Endod (2010): During endodontic procedures, oral premedication with nonsteroidal anti-inflammatory drugs (NSAIDs) resulted in an increased success rate (39%) of IANBs in teeth with IP because NSAIDs reduce nociceptor activation by decreasing the levels of inflammatory mediators. Also **Reader** reported the same results in his 2010 JOE study.

Ketorolac is a non-steroidal anti-inflammatory drug (NSAID) in the family of heterocyclic acetic acid derivatives, used as an analgesic. Ketorolac is indicated for short-term management of moderate to severe pain. It has been reported by **Yadav (JOE, 2015)** that Premedication with ketorolac significantly increases the anesthetic efficacy of articaine IANB plus infiltration in mandibular molars with IP.

Haas (retrospective study): Articaine 4% has a **5-fold higher incidence of paresthesia** compared to lidocaine.

Javier Montero (JOE, 2015): In more than 90% of patients undergoing root canal treatment, pain was totally or partially **relieved after 7 days.**

Hargreaves KM: Preoperative nonsteroidal anti-inflammatory medication for the prevention of postoperative dental pain, J Am Dent Assoc 1989. Prophylactic administration of a nonsteroidal antiinflammatory drug (NSAID), such as 200 to 400 mg of ibuprofen **30 to 60 minutes before the procedure**, has been shown to **reduce** or prevent posttreatment dental pain.

Hargreaves KM: Comparison of oral triazolam and nitrous oxide with placebo and intravenous diazepam for outpatient premedication. Oral Surg Oral Med Oral Pathol 1993.
Triazolam (0.25mg) appears to be a safe, effective alternative to parenteral sedation with a benzodiazepine for dental outpatients. **Benzodiazepines work by increasing the efficiency of a natural brain chemical, GABA, to decrease the excitability of neurons**. This reduces the communication between neurons and, therefore, has a calming effect on many of the functions of the brain.

Khan AA, Dionne RA. COX-2 inhibitors for endodontic pain. Endodontic Topics 2002.
It is now believed that COX-1 is responsible for the immediate prostanoid response and COX-2 then contributes as inflammation progresses. Thus, **COX-1 is now thought to play a role in inflammation**.

While it is clear that COX-2 inhibitors offer some advantages over the non-selective NSAIDs in terms of a lower risk of GI toxicity with long-term use, the effects following short-term use are still unclear. Until more data are available, COX-2 inhibitors should be avoided or used with the same caution as conventional NSAIDs in patients with compromised renal and cardiac function.

A recent development in pain research is the identification of a variant of COX-1, which has been named COX-

3. COX-3 was first identified in the canine brain and its activity is inhibited by acetaminophen as well as NSAIDs such as ibuprofen. The identification of COX-3 may explain the mechanism of action of acetaminophen. Acetaminophen is a centrally acting drug with a potent antipyretic and analgesic effect and a weak anti-inflammatory effect. It is now clear that acetaminophen acts by inhibiting COX-3 activity in the brain. COX-3 differs in its pharmacological activities from both COX-1 and COX-2 and is a potential target for analgesic and antipyretic drugs.

Acetaminophen alone or in combination with a low-potency opioid does have mild anti-inflammatory properties and has been shown to be effective in both acute and chronic inflammatory conditions. While acetaminophen has been considered to be the safest non-narcotic analgesic in chronic kidney disease CKD patients, it must be cautioned, however, that it may be nephrotoxic with chronic high dose use. With the exception of methadone, the majority of opioids recommended for both moderate and severe pain undergo hepatic biotransformation and renal excretion as the primary route of elimination. The significant renal retention of active or toxic metabolites of commonly used opioids including, but not limited to, morphine, oxycodone and propoxyphene can occur among advanced CKD patients and lead to profound central nervous system and respiratory depression and hypotension.

NSAIDs may be tolerated in patients with mild chronic liver disease, but they should be avoided in all patients with cirrhosis because of the increased risk of hepatorenal syndrome and the dire consequences relating to this complication. The safety of Acetaminophen was assessed in a review study by **Aminoshariae (JOE, 2015).** Acetaminophen is still the preferred analgesic in patients with **liver disease** because of the **absence of platelet impairment associated with NSAIDs.** In general, NSAIDs should be avoided in patients with liver disease. Although no consensus has been reached on what is a safe dose, the total **daily dose should not increase 2 g for patients with liver damage. Acetaminophen remains the drug of choice for these patients.**

In patients taking **lithium** NSAIDs should be prescribed cautiously due to decrease kidney excretions of lithium and possible lithium toxicity. In this case it is better to prescribe Tylenol **(Wynn, Ragheb)**

Baumgartner & Foad discussed the **antibiotic indications** in dental infections: They recommended that antibiotics are indicated when signs and symptoms suggest systemic involvement such as high fever, malaise, cellulitis, unexplained trismus, and persistent and progressive infections, and also for patients who are immunologically compromised. In this case, it can be concluded that well-localized vestibular abscess in otherwise healthy patients does not need antibiotic.

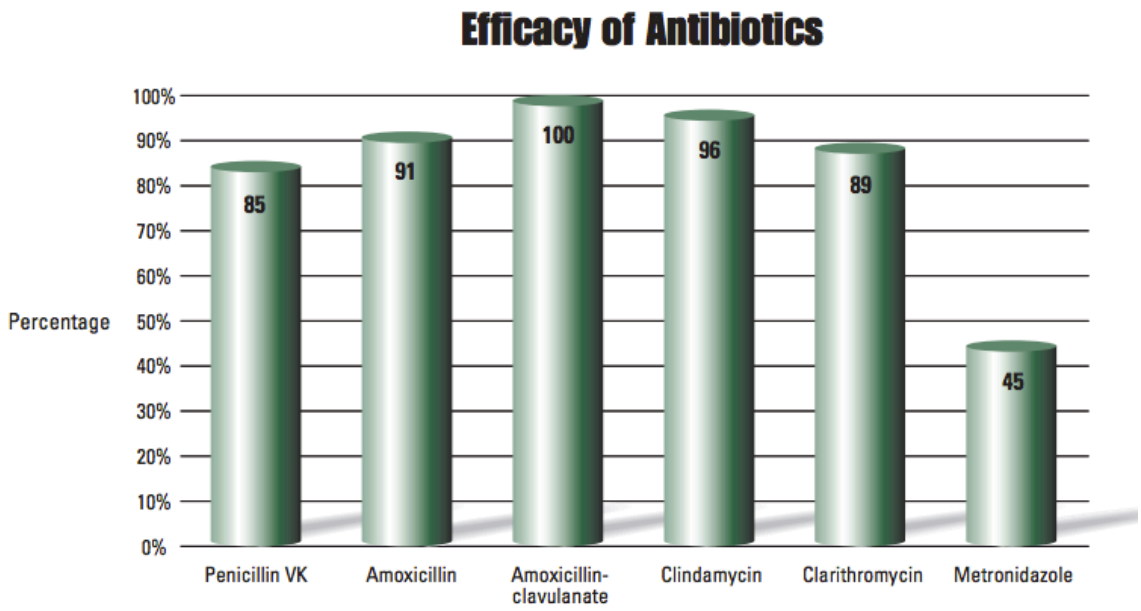
In cases antibiotics are indicated; Pen 1000mg (loading dose) is starting dose and then 500mg 4 times a day for 5-6 days. If they are allergic, Clindamycin 600 mg loading dose and then 300mg.

Neringa Skucaita 2010 (JOE) investigated Susceptibility of Endodontic Pathogens to Antibiotics in Patients with Symptomatic Apical Periodontitis. Streptococci and obligate anaerobes were the predominant microorganisms in cases of primary infection. Enterococcus faecalis dominated in cases of secondary infection. **All tested microorganisms were highly sensitive to penicillin G, amoxicillin, and ampicillin**. Susceptibilities to clindamycin and erythromycin were 73.8% and 54.7%, respectively. About 40% of the isolates were resistant to tetracycline. More than 50% of all anaerobes were resistant to metronidazole. **All E. faecalis isolates were resistant to clindamycin. Based on the study results, penicillin and amoxicillin are suitable antibiotics for treatment of endodontic infection**

Bumgartner (2003, IEJ): Pen V is still AB of choice for infections. The percentages of susceptibility for the 98 species were penicillin V (more acid stable and can be taken orally compared to g): (85%), amoxicillin: (91%), amoxicillin + clavulanic acid: (100%), clindamycin: (96%), and metronidazole: (45%). Metronidazole

had the greatest amount of bacterial resistance; however, if it is used in combination with penicillin V or amoxicillin, susceptibility of the combination with penicillin V or amoxicillin increased to 93% and 99%, respectively. Clarithromycin seems to have efficacy, but it is still considered an antibiotic under investigation because the minimum inhibitory concentration has not been established.

From Endodontic Colleagues for Excellence (2006):



DeRossi: The only known antibiotic that interfere with **OCP** and reduce effectiveness is **rifampin** due to **activation of Cytochrome P 450**. Other mechanism that can affect the OCP are interfere with absorption and OCP protein bindings. **Although the only AB know to interfere is Rifampin still we should warn female to use additional barriers for 1 week after use of AB.**

Hagai (JADA 2015): Pregnancy outcome after in utero exposure to local anesthetics as part of dental treatment. Results suggest that use of dental local anesthetics, as well as dental treatment during pregnancy, do not represent a major teratogenic risk

Drug Safety in Pregnancy (https://cced.cdeworld.com/courses/4613-Drug_Therapy_for_the_Pregnant_Dental_Patient)

Updated Drugs and Pregnancy Categories

Generic Name	Brand Name	Pregnancy Category	Potential Risk
Local Anesthetics			
Articaine with epinephrine	Septocaine	C	
Bupivacaine with epinephrine	Marcaine	C	Fetal bradycardia
Lidocaine with epinephrine	Xylocaine	B	
Mepivicaine plain	Carbocaine	C	Fetal bradycardia
Mepivicaine with levonordefrin	Carbocaine with Neo-Cobefrin	C	
Prilocaine plain	Citanest	B	Potential methemoglobinemia
Prilocaine with epinephrine	Citanest Forte	C	Potential methemoglobinemia
Benzocaine Topical	Orajel	C	Potential methemoglobinemia
Peripherally Acting Analgesics			
Acetaminophen	Tylenol	B	
Aspirin	Bayer	C/D[3]	Postpartum hemorrhage; premature closure of ductus arteriosus
Ibuprofen	Advil, Motrin	B/D[3]	Postpartum hemorrhage; premature closure of ductus arteriosus
Ketorolac	Toradol	B/D[3]	Postpartum hemorrhage; premature closure of ductus arteriosus
Naproxen	Aleve, Anaprox	B/D[3]	Postpartum hemorrhage; premature closure of ductus arteriosus
Centrally Acting Opioid Analgesics			
Codeine with Acetaminophen	Tylenol with Codeine	C/D[3]	Neonatal respiratory depression and opioid withdrawal
Hydrocodone with Acetaminophen	Vicodin	C/D[3]	Neonatal respiratory depression and opioid withdrawal
Hydrocodone with Ibuprofen	Vicoprofen	C/D[3]	Neonatal respiratory depression and opioid withdrawal
Oxycodone	Oxycontin	B/D[3]	Neonatal respiratory depression and opioid withdrawal
Oxycodone with Acetaminophen	Percocet	C/D[3]	Neonatal respiratory depression and opioid withdrawal
Oxycodone with Ibuprofen	Combunox	C/D[3]	Neonatal respiratory depression and opioid withdrawal; premature closure of ductus arteriosus
Tramadol	Ultram	C	

Antibiotics			
Amoxicillin	Amoxil	B	
Amoxicillin and Clavulanate	Augmentin	B	
Azithromycin	Zithromax, Z-Pack	B	
Cephalexin	Keflex	B	
Clindamycin	Cleocin	B	
Doxycycline	Doryx	D	Tooth discoloration and inhibition of bone development
Erythromycin base	E-mycin	B	Avoid estolate salt
Fluconazole	Diflucan	C	Fetal brachycephaly, cleft palate, thinning of bones
Gentamicin	Garamycin	C/D[3]	Ototoxicity potential in fetus
Metronidazole	Flagyl	B	
Minocycline	Dynacin, Minocin	D	Congenital anomalies and enamel hypoplasia
Penicillin V	Pen-Vee K	B	
Tetracycline	Tetracycline generic	D	Maternal hepatoxicity and enamel hypoplasia; tooth discoloration
Sedatives/Anxiolytics			
Alprazolam	Xanax	D	Congenital malformations, withdrawal symptoms
Diazepam	Valium	D	Congenital malformations, withdrawal symptoms
Lorazepam	Ativan	D	Congenital malformations, withdrawal symptoms
Midazolam	Versed	D	Congenital malformations, withdrawal symptoms
Triazolam	Halcion	X	Congenital malformations, withdrawal symptoms
Other			
Diphenhydramine	Benadryl	B	
Epinephrine	Epinephrine	C	Potential for fetal hypoxemia
Flumazenil	Romazicon	C	Avoid during labor and delivery
Phentolamine	OraVerse	C	Avoid during labor and delivery

D[3] = Avoid in third trimester. Designated D[3] drugs are considered Pregnancy Category D when taken in third trimester.

Single visit Vs. Multiple visits:

Regarding Single Vs. Multiple visits it can be noticed that must of the classic literatures emphasize on importance of multiple visits using intra canal medicaments. However, in more recent articles it has been confirmed that there is no significant difference regarding the success rate and post op pain between single and multiple visits. This might be attributed to the fact that in recent studies more advanced technologies like rotary files and irrigation systems are used which enhance the antimicrobial properties of chemo mechanical preparation.

Single visit Vs. Multiple visit: still a dilemma!! In 2011(JOE) Yingying Su performed **a systematic review** and suggested that the healing rate of single- versus multiple-visit root canal treatment was similar for infected teeth. The prevalence of post-obturation pain was significantly lower in single-visit approach at short-term follow-up time. However, because the number of studies included in this review was limited, it might be preliminary to conclude that there is no difference between single- and multiple-visit root canal treatments in terms of postoperative complications for teeth with infected root canals

Fava LR: If a canal has been entered, the clinician should be committed to removing all tissue. Partial instrumentation (i.e., leaving tissue remnants in the canal) may result in increased post-treatment pain.

Nair: Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after "one-visit" endodontic treatment (2005). The results showed (1) the anatomical complexity of the root canal system of mandibular first molar roots and (2) the organization of the flora as biofilms in **inaccessible areas** of the canal system that cannot be removed by contemporary instruments and irrigation alone in one-visit treatment. These findings demonstrate the importance of stringent application of all nonantibiotic chemo-mechanical measures to treat teeth with infected and necrotic root canals so as to disrupt the biofilms and reduce the intraradicular microbial load to the lowest possible level so as to expect a highly favorable long-term prognosis of the root canal treatment.

Francisco Wanderley Garcia Paula-Silva, Léa Assed Bezerra da Silva (JOE, 2010): Teeth with apical periodontitis that had root canal therapy performed in a single visit presented an **intense inflammatory cell infiltrate.** Periapical tissue was extremely disorganized, and this was correlated with the presence of bacteria. Higher MMP expression was evident, similar to teeth with untreated apical periodontitis. In contrast, teeth with apical periodontitis submitted to root canal treatment with calcium hydroxide presented a **lower inflammatory cell infiltrate.** This group had moderately organized connective tissue, lower prevalence of bacteria, and lower number of MMP-positive cells, similar to healthy teeth submitted to treatment. Teeth treated with calcium hydroxide root canal dressing exhibited a lower percentage of bacterial contamination, a lower MMP expression, and a more organized extracellular matrix, unlike those treated in a single visit. **This suggests that calcium hydroxide might be beneficial in tissue repair processes.**

A comprehensive analysis was performed by **Jorge Paredes-Vieyra (JOE,2012)** regarding a success rate of 1 visit compared to 2 visits in a **2 years prospective study**. In the 1-visit group, 141 of 146 teeth (96.57%) were classified as healed as compared with 121 (88.97%) of 136 teeth in the 2-visit group. Eleven cases were classified as uncertain in the 2-visit group (8.08%) compared with 4 (2.73%) in the 1-visit group. The difference between groups were **NSD**. Several factors play an important role in the decision-making process of 1- versus 2-visit endodontics. Among these are objective factors like preoperative diagnosis, the ability to obtain infection control, root canal anatomy, procedural complications, and subjective factors like patients' signs and symptoms. This study provided evidence that with a treatment protocol with proper instrumentation and irrigation can lead to healing in cases of apical periodontitis.

Figini L: Single versus multiple visits for endodontic treatment of permanent teeth: **Cochrane systematic review. J Endod 2008**: Systematic review found that there was **no detectable difference in the effectiveness of root canal treatment in terms of radiologic success** between single and multiple visits. Neither single-visit nor multiple-visit root canal treatment can prevent 100% of short-term and long-term complications. The review found that the incidence of post-obturation discomfort was similar in the single- and multiple visit approaches although analgesic use was significantly less common in patients undergoing multiple-visit root canal treatment.

Eleazer et al: NO DIFFRENCE in post op pain of necrotic teeth in single visit compared to multiple visit.
Oliet confirmed these findings.

Yoldas et al 2004: single visit retreatments had higher flare ups than multiple visits Take all stuff out, get patency, create space for CaOH and then leave it for the second visit.

Two classic studies Sjogren and Trope have questioned the long-term prognosis of single visit treatment, especially in cases of acute periodontitis. Teeth with nonvital pulps and apical periodontitis are often more complex than vital cases. Agreement is lacking concerning the appropriateness of single-visit endodontics for treating these patients. Some have postulated that the inter visit use of an antimicrobial dressing is essential to thoroughly disinfect the root canal system. Agreement is lacking concerning long-term success rates associated with single-visit and multivisit procedures. **Sjögren** and associates investigated the influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. Periapical healing was observed 5 years after completion of treatment. They concluded that “Complete periapical healing occurred in 94% of cases that yielded a negative culture. When the samples were positive before root filling, the success rate of treatment was just 68%—a statistically significant difference.” They concluded that the objective of eliminating bacteria from the root canal system “cannot be reliably achieved in a one-visit treatment because it is not possible to eradicate all infection from the root canal without the support of an interappointment antimicrobial dressing.” However, the findings of **Friedman, Weiger and colleagues and Peters and Wesselink** do not support Sjögren and colleagues. Those studies found no statistically significant differences in healing between teeth, with apical periodontitis, treated in one visit and two visits with the inclusion of calcium hydroxide as an intravisit medication.

Molander A: Clinical and radiographic evaluation of one- and two-visit endodontic treatment of asymptomatic necrotic teeth with apical periodontitis: a randomized clinical trial. J Endod, **2007**. **Fitzgerald PI:** Outcome of one-visit and two-visit endodontic treatment of necrotic teeth with apical periodontitis: a randomized controlled trial with one-year evaluation. J Endod **2008**: Both studies have found no statistically significant difference in success when using the single-visit or multivisit approach to the nonvital tooth with apical periodontitis.

Sathorn (2005, IEJ) conducted a systematic review of single- versus multiple-visit endodontic treatment of teeth with apical periodontitis. They found that, on the basis of current best available evidence, single-visit root canal treatment appeared to be slightly more effective than multiple-visit treatment (6.3% higher healing rate). However, the difference between these two treatment regimens **was not statistically**. This is a complicated issue because the inability to detect differences between groups might also be due to variations in research methodology, including sample size, duration of follow-up, and treatment methods.

Postoperative Pain in Multiple-visit and Single-visit Root Canal Treatment (Abdel Hameed H. ElMubarak- JOE 2010): The overall incidence of postoperative pain was 9.0% after 12 hours and 24 hours. Postoperative pain developed in 15.9% of the patients with history of preoperative pain, whereas 7.1% had postoperative pain among those without history of preoperative pain. There was no significant difference in postoperative pain between single-visit and multiple-visit root canal treatment (RCT).

Prognosis and success rate:

Review of cause of failure:
1) Interradicular infection: **Nair 1990**
2) Extraradicular infection: **Sundqvist 1980, Sjorgren 1988,1997, Wayman, Tornstad**; These failure cases are not amenable to re-tx and need surgery.
3) Foreign body reaction: **Koppang 1989, Nari 1990, Sjogren 1995**
4) Cysts: **Nair 1990**
5) Fibrous scar tissue: **Nair 1999**

Materials used in non-surgical root canal treatment (**Nair et al. 1990b, Koppang et al. 1992**) and certain food particles (**Simon et al. 1982**) can reach the periapex, induce a **foreign body reaction** that appears radiolucent and remain asymptomatic for several years (**Nair et al. 1990b**).

Prognostic factor in root canal treatment **(Shimon Freidman):**

Many studies have investigated the outcome of root canal treatments and there are some factors which might affect the results of these studies. We should always consider these factors while interpreting the results:

1) Type of teeth in study
2) Number of subjects that considering many confounding factors (200 is too small)
3) proportion of teeth with apical periodontitis and retx cases
4) Criteria for case selection that affect the success rate (Ingle)
5) Operators
6) Asepsis and use of rubber dam
7) Intracanal medicament and procedures
8) Post RCT restoration.

Generally, when reviewing articles which have assessed the success rate of RCT, Prognostic factors have been divided to 3 main groups:

1) **Preoperative factors:**

-Apical periodontitis: success rate is 10-25% lower.
-Lesion size: some studies indicate a better prognosis for apical periodontits lesion 2-5mm than for larger **(Friedman, Strindberg).** However, some studies did not find significant difference **(Sjogren).**
- Pulpal status: The success rate of vital teeth is shown to be higher or comparable **(Freidman, Kerkes &Torsntad).**
-Periodontal statues: does not affect the success rate **(Sjogren).**
-Age, gender showed no effect on the success rate.

2) **Intraoperative factor:**

-Apical extent of canal instrumentation and filling: Extrusion of filling materials beyond the root-end generally result in poorer treatment outcome (**Bergenholtz, Seltzer and Strindberg**). However, **Sjogren** believed that extrusion just impaired the outcome in infected cases.
GP is well tolerated by body per se therefore its extrusion can not affect the success rate per se. However, extrusion of GP is usually followed by overinstrumentation and extrusion of bacteria which in case impair the

healing rate (**Sojgren**). It has also been reported that extrusion of filling materials is totally or partially removed by the surrounding tissue (**Augsburger**).
Studies correlated short root filling (more than 2mm) with reduced success rate. However, **Sjogren** found that short fillings are just associated with reduced hilling rate in infected cases.
Friedman showed that fillings 0-2mm from the apex show higher success rate than short or overfilled.

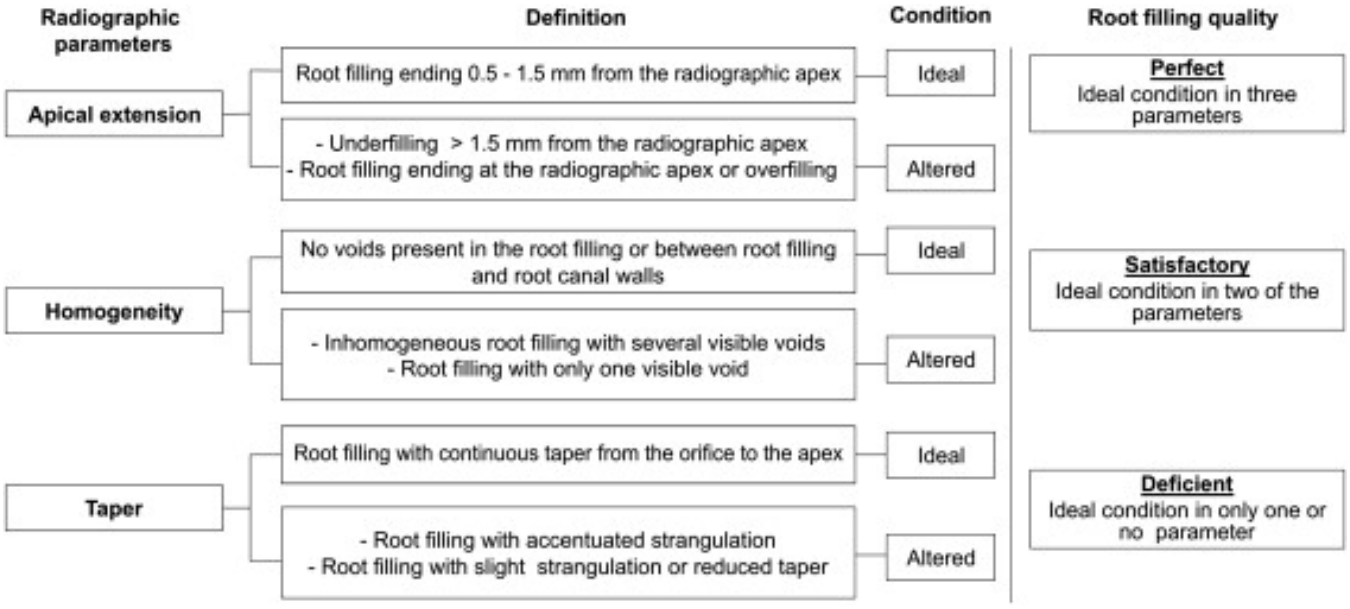
-Apical enlargement: **Yared & Budahger** and also **Orstavik** proposed that apical enlargement promotes effective disinfection of the apical portion of the canal.
- Treatment sessions: debate in Endo
-Materials and techniques: **Strindberg** found no difference in the success rate using different sillers. **Friedman** Found higher success rate using flared technique and vertical condensation compared to standard step back and latera condensationl.
-Void in obturaion and Sealer extrusion: **Friedman** found no effect on success rate

3) Post operative factors:
-Restoration

Aquilino & Caplan (2002): teeth without crown lost at 6X higher rate. The final Cox model showed that endodontically treated teeth not crowned after obturation were lost at a 6.0 times greater rate than teeth crowned after obturation

Moreno JOE 2013: Canals filled up to 0–2 mm short of the apex had a significantly higher number of teeth rated as healthy than overfilled or underfilled cases. Regression analysis showed that the quality of endodontic treatment was the most significant factor influencing the periradicular status ($P < .001$).

Keep in mind that in many studies evaluating the quality of the RCT and prevalence of periodontitis or out come of RCT there are 3 parameters which have been considered in most of the articles: They are 1) apical extension of root filling 2) quality and homogeneity of root filling and 3) taper **(Hasselgren, 2007 IEJ ; Tavares 2009 JOE ; Santos 2010 JOE ; Yu-Hong Liang 2011 JOE**). **Following chart from Santos et al (JOE, 2010) study can be a clinical guide for root canal quality assessment.**



Interesting findings in **Liang (2011, JOE)** study showed that different factors in PA assessment and CBCT assessment can affect the outcome of root canal treatment. When findings from PA were analyzed density and apical extent of root filling were identified as predictors ($p < .05$). When findings from CBCT were analyzed, density of root filling and quality of coronal restoration significantly influenced treatment outcome ($p \leq .001$). **This might be explained by the fact that 80% of root fillings which were considered over in PA were actually flush fillings (0-2 mm of apex) on CBCT images.**

Gomes (Brasil, JOE,2015): A significant difference was observed when comparing the treatment outcome for teeth with and without **coronal restorations**. The odds ratio allowed the conclusion that it is 0.6 times most probable to observe a healthy periapical condition when you have the presence of coronal restoration when compared with an absence of coronal restoration. Regarding the **apical extension** of the filling, the best results were observed for canals filled within to 0–2 mm short of the apex, with a statistically significant difference over teeth with over- or underfilling ($P < .0001$). The analysis of the odds ratio showed that it is 4.68 times more likely to find healthy teeth when the apical extension of the filling is 0–2 mm short compared with teeth with overfilling. **The apical extent of the filling >2 mm short from the foramen also displays an odds ratio of 2.024, which corresponds to a significantly higher possibility of finding healthy teeth compared with overfilling.**

Victoria Soo Hoon Yu in 2012 (JOE) assessed the **lesion progression in post-treatment Endo lesions**. Recall **lesion size** greater than 5 mm in diameter posed the highest relative risk (RR) at 2.9 times (95% confidence interval [CI], 1.9–4.6; P < .0005) compared with lesions less than 2 mm in size. The presence of **biting pain** at recall indicated a 1.8-times increase (95% CI, 1.2–2.6; P = .002) in the risk of lesions not improving. A history of a **flare-up** any time after obturation increased the risk of lesions not improving by 1.5 times (95% CI, 1.1–2.0; P = .014). A **root filling** without an ideal working length was 1.4 times more likely (95% CI, 1.0–2.0; P = .046) to be associated with a lesion that did not improve over time.

Eleazer JOE, 2010: Comparison of Classic Endodontic Techniques *versus* Contemporary Techniques on Endodontic Treatment Success: This study compared the survival rates of endodontic treatment performed by using classic techniques (eg, instrumentation with stainless steel hand files, alternating 5.25% NaOCl and 3% H_2O_2 irrigation, mostly **multiple treatment visits**, and so on) versus those performed using more contemporary techniques (eg, instrumentation with hand and rotary nickel-titanium files, frequent **single-visit treatment**, NaOCl, EDTA, chlorhexidine, H_2O_2 irrigation, warm vertical or lateral condensation obturation, use of surgical microscopes, electronic apex locators. Of the 459 teeth in the classic group, there was an overall survival rate of 98% with an average follow-up time of 75.7 months. Of 525 teeth in the contemporary group, there was an overall survival rate of 96%, with an average follow-up time of 34 months. Considerably more treatments in the classic group were completed in multiple appointments (91%) than in the contemporary group (39%). More teeth in the classic group underwent post-treatment interventions (6.7% vs 0.9%, respectively).

Sjogren, Hagglund, Sundqvist and Wing 1990 JOE
PROGNOSIS!! - Diagnosis Drives Prognosis or Prognosis is driven by Diagnosis

Vital teeth: 96% success rate – no microorganisms
PN(necrosis)-PL (lesion): 86%
PN-PL with overfill than 2mm: 76%
PN-PL under fill more than 2 mm: 68%

Sjogren (1997) reduced success when bacteria are present during obturation **(94% vs 68%).** They suggested three negative culture before obturation increase the success rate. In contrary to **Bender and Seltzer**: Culturing didn't affect outcome

Success rate based on Phase 3 Toronto study (**Friedman**):
-Teeth with no previous lesion had 93% success. However, teeth with lesion (CAP) showed 80% success.
-89% total success for Warm vertical condensation FPVC: Flared preparation / vertical compaction.
-73% total success for Lateral condensation SBLC: Step Back Lateral Compaction.

Studies showing reduced success of NSRCT with apical periodontitis:
Success (%): **Sjogren (1990)** 96% compared to 86% **& Friedman (1995)** 93% compared to 69%

Hoskinson SE, Ng YL, Hoskinson AE: OOOO 2002: In this study the presence of a pre op lesion was the biggest prognostic factor; **success rates decreased by 18% for every 1-mm increase in size of a pre-operative periapical lesion.**

Ricucci D, Siqueira JF Jr. J Endod. 2010: Biofilms and apical periodontitis: study of prevalence and association with clinical and histopathologic findings. ⇑larger lesion ⇒ ⇑more biofilm. size of the periapical lesion was factors that had a negative influence on the prognosis.

Nadia Chugal 2003: in teeth with necrotic pulp best outcome was observed with root fillings at 0.55 mm short from radiographic apex. In teeth/roots with apical periodontitis, a millimeter loss in working length increased the chance of treatment failure by 14%. The risk of failure was higher for a fair/poor density of obturation than for a good density for all diagnoses of periradicular status.

Ng YL: Outcome of primary root canal treatment: systematic review of the literature. Part 2. Influence of clinical factors. Int Endod J 2008
A systematic review of the literature examined the success and failure of nonsurgical endodontic therapy. The authors concluded that four conditions (**pretreatment absence of a periapical radiolucency, root filling with no voids, root filling extending to 2 mm within the radiographic apex, and satisfactory coronal restoration**) were found to improve the outcome of primary root canal treatment. They went on to note that the results of the review "should be interpreted with caution and cannot be considered to give definitive conclusions because of the retrospective and heterogeneous nature of the data. It does, however, provide strong clues about the factors likely to dominate outcomes and inform the design of future randomized trials."
Ng: In Ng study 83**% success rate** for NSRCT and 80% ReTx was reported. Eleven prognostic factors were identified. The conditions that were found to improve periapical healing significantly were: the preoperative absence of a periapical lesion (P = 0.003); in presence of a periapical lesion, the smaller its size (P=0.001), the better the treatment prognosis; the absence of a preoperative sinus tract (P = 0.001); achievement of patency at the canal terminus (P = 0.001); extension of canal cleaning as close as possible to its apical terminus (P = 0.001); the use of ethylene-diaminetetra-acetic acid (EDTA) solution as a penultimate wash followed by final rinse with NaOCl solution in 2!RCTx cases (P = 0.002); abstaining from using 2% chlorexidine as an adjunct irrigant to NaOCl solution (P = 0.01); absence of tooth/root perforation (P = 0.06); absence of interappointment flare-up (pain or swelling) (P = 0.002); absence of root-filling extrusion (P=0.001); and presence of asatisfactory coronal restoration (P=0.001).

In a systematic review by **Ng investigated tooth survival after RCT**; 14 studies met the inclusion criteria. Four key factors were identified as enhancing the survival of teeth after RCT: the **presence of interproximal contacts, no plans for using the treated teeth as abutments for fixed or removable partial dentures**, tooth **type**, and **crown restoration.**

Orstavik and pitt-ford 1998: The goal of RCT is to prevent and cure apical periodontitis. Also they suggested Peri apical index for periapical assessment: 500 teeth, follow up 1, 2, 4 years, PAI scoring.
Follow up recommendation of vital cases: 1year. Most cases of failures were detected within 1 year. **70% of new CAP will appear in 1 year**. 90% in 2 years. Full CAP healing: 50% in 1 year, 80% 2 years, 90% 3 years **Partial healing of CAP 90% in 1 year.** 76% of apical periodontitis lesions develop post are seen in 1 year. **Therefore, follow up of 1 year predict long term success.**

Strindberg 1956: Histological success most difficult to achive!!
Strindberg success criteria: Absence of radiolucency, PDL not more than 1.5 times normal, lamina dura intact, no symptoms, no swelling, no sinus tract, no pain on percussion or palpation, absence of PARL
Healing in some cases took until 10 years to heal. Recommendation of 4 year follow up for necrotic cases
Vital cases had 95% success; Necrotic had 71% success after 4 years, if extended to 10 years 85% success.
Lower success rate if there is a lesion.

Rud & Andreasen 1972: Watch periradicular area for **1yr**. If **healed or healing** at 1yr, then healing is ok. If not, then re-tx.

Andreassen & Rud 1972: It is difficult to determine if a large PARL is scar tissue or inflammation in the healing periapical surgery area. It is more common in Max anterior

Molven, Halse, Grung 1996 (Norway / JOE): Lateral incisor most often found with scar tissue. The findings support the conclusion that cases clearly showing features of incomplete healing (scar tissue) at the regular follow-up 1 yr after surgery can be regarded as successes. They need not be recorded for further systematic control.

Torabinejad, Anderson and bader (2007): Success rates for implant supported crown (ISCs) were higher than for RCTs and FPDs, respectively; however, success criteria differed greatly among treatment types, rendering direct comparison of success rates futile. **Long-term survival rates for ISCs and RCTs were similar and superior to those for FPDs.**

Iqbal, kim: Outcomes were similar in primary RCT and implant (high 90's): The **decision to treat a compromised tooth endodontically or replace it with an implant must be based on factors other than treatment outcome.**

Torabinejad (2015, JOE) performed a **meta-analysis** to evaluate the success rate of **intentional replantation Vs. implant supported crown**. Meta-analysis revealed a weighted mean survival of 88% (95% CI, 81%–94%) for IR teeth. Root resorption was reported with a mean prevalence of 11%. The weighted mean survival of ISCs was 97% (95% CI, 96%–98%). The mean survival of ISCs was significantly higher than that of IR teeth ($P <$ .001). A recent study on IR teeth indicated that orthodontic extrusion before intentional replantation improved survival rates.

One of the factors that can significantly affect the treatment modalities is quality of life. In 2011 (JOE) study by Dustin L. Gatten both RCT and implant supported crowns showed **similar overall OHIP scores** and show a high rate of satisfaction with both treatment modalities. In addition to the prognosis and outcomes, clinicians should consider patients' perceptions and preferences as well as the influence each therapy may have on their quality of life, both short- and long-term.

Salehrabi & Rotstein 2010, JOE
1,463,936 RCT treated teeth followed up to **8** years (**Delta Dental insurance**)
97% of the RCT treated teeth were **retained** within this 8year period; This finding does not reflect success rate.
3% had re-treatments, apical surgeries or extractions mostly within 3years
85% of the extracted teeth had no full coronal coverage.

Surgery:

"Root-end resection cannot compensate for poor orthograde endodontic treatment. In a retrospective evaluation, **Abramovitz** found that only 45% of the teeth that were referred for apical surgery were adequately selected. In addition, 83% of the teeth from this evaluation were found to be inadequately obturated and required nonsurgical retreatment instead of apical surgery. **Thus, teeth that present with postsurgical pathosis often lack proper orthograde endodontic treatment".**

After failed primary root canal treatment, **orthograde retreatment should always be considered first instead of apical surgery**. When a patient present with post-treatment disease in a tooth in which apicosurgery had already been performed instead of orthograde retreatment, the endodontist must still come up with a treatment plan.

Better orthograde treatment choices and
case selection enhances the success of surgical
therapies in cases with previous post-treatment disease
(Zuolo et al. 2000).

Johannes Mente (JOE, 2015) evaluated the treatment outcomes of **nonsurgical retreatment after a failed apicoectomy** clinically and radiographically. It should be considered that in the included cases, apical surgery had been performed instead of regular retreatment in failure cases. Based on the result, twenty teeth (87%) were classified as "success," and 3 teeth were considered (17%) "failure after non surgical retreatment following failed surgery.

Tooth Retention through Endodontic Microsurgery (EMS) or Tooth Replacement Using Single Implants (SI): A Systematic Review of Treatment Outcomes (Torabinejad JOE, 2015)

Survival Rates: SI survival rates varied from 96% at 2–4 years to 98% for 6+ years; This indicated that implant losses primarily occurred before 2 years, with few being lost thereafter; a steady state was approached within the times studied. Teeth treated using EMS had survival rates of 94% at 2–4 years and 88% at 4–6 years, indicating that teeth treated with EMS tended to be lost at low rates over the time studied. Teeth treated using EMS substantially lagged the survival of SIS at the 2- to 4-year time interval. Survival data for 6+ years were not identified.

Success Rates: A comparison between SI and EMS success rates was not appropriate because the success criteria for the different treatment modalities were qualitatively different. SI success rates varied from 98% at 2–4 years to 97% at 6+ years;. Implants that had been successful at 2–4 years tended to remain as successes for the duration of the period studied; a steady state was attained. Teeth treated with EMS had success rates of 90% at 2–4 years and 84% at 4–6 years; the CIs barely overlapped, suggesting a tendency for teeth treated with EMS to become unsuccessful over time. EMS success data for 6+ years were not identified.SI success rates did not differ from SI survival rates for each of the 3 time periods studied. In contrast, EMS success rates were lower than EMS survival rates for both time periods studied.

Evidence Summarizing Endodontic Microsurgery Survival and Success Rates:

Author	Years of follow-up	Survival rate (%)	Success rate (%)
Rubinstein and Kim	7	92	92
Chong et al	2	95	90
Taschieri et al	2	94	91
Taschieri and Del Fabbro	2	93	91
Taschieri et al	4	91	88
von Arx et al	5	87	76

One of the challenging situations following a failed RCT tooth is that a tooth should be retreated nonsurgically or surgically, or should the tooth be extracted and replaced with an implant-supported restoration or fixed partial denture. **In a cost-effectiveness analysis by kim (JOE, 2011)** it was mentioned that **Endodontic microsurgery was the most cost-effective approach followed by nonsurgical retreatment and crown, then extraction and fixed partial denture, and finally extraction and single implant–supported restoration.** A single implant–supported restoration, despite its high survival rate, was shown to be the least cost-effective treatment option based on current fees.

Different studies have evaluated the prognostic factor that affect the outcome of surgery. **Age of the patient, existing root-filling length, preoperative lesion size, and apical and coronal seal are the main factors mentioned in different studies.** This inconsistency may be caused by the differences in the technical quality of periapical surgery as well as case selection, sample size, the observation period, and methodology (Friedman, Rahbaran). **In a recent study by Song (2011, JOE) age, sex (female), tooth position (anterior), root-filling length (adequate), lesion type (endodontic lesion), root-end filling material (mineral trioxide aggregate and Super EBA; Harry J. Bosworth, Skokie, IL), and restoration at follow-up appeared to have a positive effect on the outcome.**

A meta-analysis (Tsesis, JOE, 2013) was performed to assess the 1 year success rate of surgical Endodontic treatment performed by modern techniques (MICROSCOPE, NON BEVELED ROOT END PREPARATION) From the meta-analysis of the 18 studies, the pooled percentages of success (complete healing and incomplete healing), uncertain healing, and failure at the 1-year follow-up were found to be **89.0%,** 4.6%, and 6.4%, respectively. **MTA was significantly associated with better treatment outcomes** than other retrofilling materials. The use of IRM provided significantly worse outcomes compared with MTA ($P < .05$) or EBA ($P < .05$) in the low risk of bias studies but not in the high risk of bias studies ($P > .05$). Finally, the use of EBA was associated with less favorable outcomes compared with the use of MTA in the high risk of bias ($P < .05$).

Kim (JOE, 2013) suggested that the height of the buccal bone plate was the only significant predictor (P = .040) of the healing outcome, suggesting that **teeth with a buccal bone plate >3 mm presented a higher success rate than teeth with a buccal bone plate that was ≤3 mm high** (94.3% vs 68.8%,P < .001).

Kim: The best method of controlling hemorrhage is to establish **hemostasis before flap reflection**. This is accomplished by injecting lidocaine with 1:50,000 epinephrine at various sites in the alveolar mucosa and near the root end. The slow injection of the solution in numerous sites within the localized operative field should be accomplished even with block anesthesia because the localized effect of the vasoconstrictor is more pronounced.

Calcium sulfate (CaS) is a simple, biocompatible material with a long history of safe use in different fields of medicine. CaS is a rapidly resorbing material that leaves behind a calcium phosphate lattice, which promotes bone regeneration and hemostasis. **Antonio Scarano (JOE, 2012)** showed the higher efficacy of hemostasis compared to ferric sulfate.

Clinical Results with Two Different Methods of Root-end Preparation and Filling in Apical Surgery: Mineral Trioxide Aggregate and Adhesive Resin Composite, **Von Arx (2010, JOE):** The overall rate of healed cases was 85.5%. MTA-treated teeth demonstrated a significantly (P = .003) higher rate of healed cases (91.3%) compared with Retroplast-treated teeth (79.5%). Within the MTA group, 89.5%–100% of cases were classified as healed, depending on the type of treated tooth. In contrast, more variable rates ranging from 66.7%–100% were found in the Retroplast group.

Gagliani, F. G. M. Gorni (**IEJ, 2005)** conducted a study to monitor the outcome of periradicular surgery in teeth that had previously undergone surgical treatment. 59% healed completely, 17% were considered to have incompletely healed and 23% were associated with post-treatment disease. Surgical retreatment of teeth previously treated with surgery is a valid alternative to extraction. However, association with post-treatment disease was greater than after a primary surgical approach.

Guttman&Harrison; Kim (microsurgery) = indication of Surgery: **IF YOU CAN NOT SOLVE THE PROBLEM OR RETREATMENT IS IMPOSSIBLE; THEN SURGERY MIGHT BE INDICATED.**

Rubenstein & Kim (1999): Using **scope**, **ultrasonics** and **Super EBA** (reinforced zinc oxide cement; its liquid contains 32% eugenol and 68% ethoxy benzoic acid): n=94 cases (2/3 posterior & 1/3 anterior): 97% radiographic success at 3-12m follow-up with mean healing of 7.2m (criteria = restoration of lamina dura). 85% granuloma and 15% cysts with no difference in time to heal. Isthmuses were found in 25% of the cases.

In 2012 (JOE) KIM in a prospective randomized controlled study mentioned that there is no significant difference in the clinical outcomes of endodontic microsurgery when Super EBA and MTA were used as root-end filling materials.

Thomas von Arx (JOE, 2010) performed a **meta-analysis** regarding the prognostic factors in apical surgery:
With regard to tooth-related factors, the following categories were significantly associated with higher healed rates: cases **without preoperative pain or signs**, cases with **good density of root canal filling**, and cases with **absence or size ≤5 mm of periapical lesion**. With regard to treatment-related factors, cases treated with the use of an endoscope tended to have higher healed rates than cases without the use of an endoscope.

Harrison & Jurosky 1991 Healing of incisional flaps in rhesus monkeys.
Sulcular incision leaves perio tissue attached to cementum which speeds up repair and prevents epithelial down growth.

The incisional wound
* Few differences between sulcular and submarginal healing. Submarginal design showed less predictable results.
2) The dissectional wound:
*Scaling of root attached tissue and tags on the cortical bone should be avoided to allow rapid reattachment. Cortical retained periosteal tissues exert some protective influence which prevents necrosis of surface lamellae in underlying cortical bone.
*The elevated periosteum does not survive the flap reflection, its cambium layer do not survive but becomes depolymerized and reforms laters.
* Crestal bone osteoclastic activity occurs following submarginal and rectangular flaps. However osteoblastic repair occurs and creatal bone height is not altered.
3) The osseous excisional wound:

*osteoclastic activity not observed within the excisional wound site
*The endosteal tissue play the major role in osseous excisional wound healing
* Periosteum does not function until the excisional wound is filled with woven bone

Harrison & Jurosky 1991 Healing of osseous **excisional** wounds in rhesus monkeys.
Days 1-3: coagulum of disorganized fibrin acts as barrier to inflam/repair cells
Day 4: inflam cells in coagulum
Day 14: proliferating granulation tissue replaces coagulum, woven bone, osteocytes, dense fibrous CT spearates flap from bone
Day 28: trabeculae coalesce, lined with osteoblasts, in contact with devitalized cortical bone of wound edges

Harrison & Jurosky 1991 Healing of **dissectional** wounds in rhesus monkeys.
Day 1: have clot present;
Day 2-3: have PMNs, macrophages, fibroblasts.
Day 4: Type I collagen in new BV, fibroblasts predominate, osteoclasts.
Day 14: have fibrous CT, new periosteum, no loss of alveolar crest
Day 28: have completely normal tissue

Gilheany 1994:

Studied relationship between bevel angle of root resection and required depth of retroprep to minimize leakage:
0 degree bevel: minimal retroprep depth of 1 mm
30 degree bevel: minimal retroprep depth of 2.1 mm
45 degree bevel: minimal retroprep depth of 2.5 mm
They conclude with a recommendation of 3.5 mm retroprep depths (thus, the retroprep depth should extend coronal to the pulpal terminus of the tubules)

Friedman assessed the success rate of apical surgery in two intervals of 1 and 5 years (JOE, 2012). It was found that a total of 129 of 170 teeth were healed (75.9%) compared with 83.8% at 1 year. Two significant outcome predictors were identified: **the mesial-distal bone level** at ≤3 mm versus >3 mm from the cementoenamel junction (78.2% vs 52.9% healed, respectively) and **root-end fillings with ProRoot MTA versus SuperEBA.**

Moiseiwitsch & Trope (1998 OOO): Never jump to surgery if retx is applicable!!!

Wang N, Knight K, Dao T, Friedman S: Treatment outcome in endodontics—the Toronto Study. Phases I and II: apical surgery. Analysis indicated an increased odds ratio for disease persistence for teeth with larger pretreatment lesions and pretreatment root canal filling of adequate length. Pretreatment lesion size and root-filling length were significant predictors of the outcome of apical surgery.

Torabinejad M: Outcomes of nonsurgical retreatment and endodontic surgery: a systematic review (2009, JOE): On the basis of these results it appears **that endodontic surgery offers more favorable initial success, but nonsurgical retreatment offers a more favorable long-term outcome.**

Abou-Rass: Surgical endodontics is avoided **unless** retreatment is first attempted or the quality of previous root canal therapy is acceptable or the canal obstructed (**Finalization**)

Surgery case selection based on **Arens text book**: In case that **canal is not negotiable**, there is an **extrusion of material, severe curve, severe calcification**, **extraradicular biofilm**. In these case you **may** consider surgery before re-tx. In case of Root is excessively short, Tooth is non-restorable don't consider surgery.

Rosenberg in 2010 (JOE) published a review article on tissue regeneration: Tissue regeneration by using membrane barriers and bone grafting materials in periapical surgery is an example of tissue engineering technology. Membrane barriers and/or bone grafts are often used to enhance periapical new bone formation. However, the periapical tissues also consist of the periodontal ligament (PDL) and cementum. For regeneration of the periapical tissues after periapical surgery, one of the important requirements is recruitment and differentiation of progenitor/stem cells into committed pre-osteoblasts, pre-PDL cells, and pre-cementoblasts. Homing of progenitor/stem cells into the wounded periapical tissues is regulated by factors such as stromal cell–derived factor 1, growth factors/cytokines, and by microenvironmental cues such as adhesion molecules and extracellular matrix and associated noncollagenous molecules

Guided tissue regeneration techniques have been suggested as an adjunct to endodontic surgery in order to promote bone healing. **Tsesis (JOE, 2011) in a meta analysis** declared that GTR techniques may improve the outcome of bone regeneration after surgical endodontic treatments of teeth with certain lesions.

Anita Aminoshariae (JOE, 2014) in a critical review assessed different methods used to locate the mental foramen (Following table):

Techniques Used to Locate the MF; In courtesy of Anita Aminoshariae (JOE, 2014)

Author(s)	Technique	Location of MF	Benefit	Risk
Hazani et al, 2013	Palpation	The origin of the mentalis muscle	No equipment or radiation needed	Not precise
Guo et al, 2009	Anatomic landmark	23.34 ± 2.39 mm below the cusp tip of the second premolar	No equipment or radiation needed	Occlusal wear can cause errors
Kquiku et al, 2011	Direct visualization	Between the first and second mandibular premolars	Exact location of the MF is determined	Potential tissue/nerve injury
Phillips et al, 1990	Periapical radiograph	The position was 3.8 mm mesial to the apex of the second premolar	Equipment present and small amount of radiation required	Magnification, and failure to detect MF if it is located below the apical edge of the film
Jacobs et al, 2004	Panoramic radiograph	Detected in 94% (N = 545) but it was distinct only in 49% of the cases	Relatively small amount of radiation and the entire orofacial structure is included	Large degree of magnification and failure to detect MF when it is not clearly visible
Jacobs et al, 2002	Computed tomography	MF was detected in 100% of the cases (N = 230)	Magnification-free 3-dimensional visualization	Larger amount of radiation
Parnia et al, 2012	CBCT	MF was detected in 100% of the cases (N = 96)	Magnification-free 3-dimensional visualization	Ionizing radiation but less than conventional CT
Chau, 2009	MRI	Each assessor identified the MF on 278 and 298 oblique images of CBCT and MRI, respectively.	No ionizing radiation required and MRI detected mandibular nerve better than CBCT	Very expensive equipment and image
Mahmoud et al, 2010	Ultrasound	Consistently detected in dry mandibles	No ionizing radiation and real-time identification	Equipment not readily available

Tyler Kovisto (2011, JOE) assessed the proximity of IAN canal to mandibular molars using CBCT Root apices of the mandibular second molars are closest to the mandibular canal than other teeth. The mesial root of the second molar was closer to the nerve in female patients compared with male patients. Root apices in younger patients (<18 years) were generally closer to the mandibular canal than in older patients.

Paul Carruth (2015 JOE): Regarding location of mental foramen, 53.7% of the foramen were located mesial, 45.3% distal, and 1% coincident to the apex of the mandibular second premolar.

c

Freedland JB. Conservative reduction of large periapical lesions. Oral Surg Oral Med Oral Pathol 1970.
Describes **decompression** using polyvinyl tubing for access and irrigation of large PA lesions.
Indication of **marsupialization**:
Devitalization of adjacent teeth
Damage to anatomic structures (ian, sinus)
Loss of bony support
Parasthesia
Elderly pts where surg is risky

Systematic disease Vs. Apical periodontitis:

Multivariate logistic regression analysis (**Lopez, 2011, JOE)** showed that periapical and the number of root-filled teeth were significantly associated with diabetic status. However, keep in mind that there are many factors that can question the reliability of these cross-sectional studies!!!

Siqueira in a cross-sectional (JOE,2012) reported that AP was significantly more prevalent in untreated teeth from type 2 diabetics. This suggests that **diabetes may serve as a disease modifier of AP** in the sense that individuals with diabetes can be more prone to develop primary disease. However, findings do not confirm that diabetes may influence the response to root canal treatment because treated teeth had no increased prevalence of AP when compared with controls.

Benito Sánchez-Domínguez (JOE, 2015) assessed the association between **HbA1c levels** and prevalence of apical periodontitis. Multivariate logistic regression analysis showed that worse periapical status correlated significantly with HbA1c levels ≥6.5% in type 2 diabetic patients. HbA1c levels of diabetic patients are associated with periapical status. Data reported in the present study, together with the results of previous studies, further support a **relationship between glycemic control and periapical inflammation in diabetic patients.**

Foad 2003: Patients with diabetes have increased periodontal disease in teeth involved endodontically and have a **reduced likelihood of success of endodontic treatment in cases with preoperative periradicular lesions.**

Goerig reported that diabetic patients have slower healing of PARL.

Bender & Bender 2003: When Diabetes is under control, the healing of periapical lesions is the same as a non-diabetic patient.

Goldman (1987 MCNA): Reasons for poor wound healing & infection are hyperglycemia leading to impaired phagocytosis, chemotaxis, adherence and killing of bacteria. Also see reduced collagen synthesis, capillary in-growth, fibroblast proliferation.

Wang C et al 2011 (JOE): An increased risk of **tooth extraction** after root canal therapy was significantly associated with **Diabetes Mellitus**, **Hypertension**, and **Coronary Artery Disease** individually. Moreover, the constellation of systemic disease burden also manifests the importance in addition to other potential confounders.

Chen et al 2007 declared that hypertension decreases healing rate after RCT.

Juan José Segura-Egea 2011 JOE: The prevalence of apical periodontitis and root canal treatment was significantly higher in smoker hypertensive patients compared with nonsmoker subjects. Please notice these studies are cross-sectional with **low level of evidence!!! Many confounding factors are potentially ignored in these studies.**

It is well known that Chronic inflammation plays a crucial role in the pathogenesis and progression of atherosclerosis and at the same time promotes acute CV events such as plaque rupture and coronary thrombosis. **Cotti (JOE, 2012)** investigated the correlation between the presence of apical periodontitis and inflammatory markers of the blood like interleukins -1, -2, and -6 and found that **Patients with AP present with significantly greater blood concentrations of IL-1, IL-2 and IL-6a.** The findings obtained clearly underline the importance

of **AP as an independent variable in future CVD research** and in the development of synergic preventive approaches for both dental and systemic diseases.

In the most recent meta-analysis by Gomes (JOE, 2013) it was revealed that apical periodontitis (AP) is associated with increased levels of CRP, IL-1, IL-2, IL-6, asymmetrical dimethylarginine, IgA, IgG, and IgM in humans. These findings suggest that **AP may contribute to a systemic immune response** not confined to the localized lesion, potentially leading to increased systemic inflammation.

Pasqualini (2012, JOE): Case-Control study (Notice this kind of study can not show cause and effect relation): CHD subjects had a higher prevalence of oral diseases and lower compliance to oral preventive strategies than healthy controls. **Multivariate analysis showed a positive association between missing teeth, the number of LEOs, chronic periodontitis and CHD.**

Tatiana Hassin Rodrigues Costa (2014, JOE): Cross-sectional study using X2 and ODD ratio: Patients with chronic apical periodontitis had a 2.79 times higher risk of developing coronary artery disease.

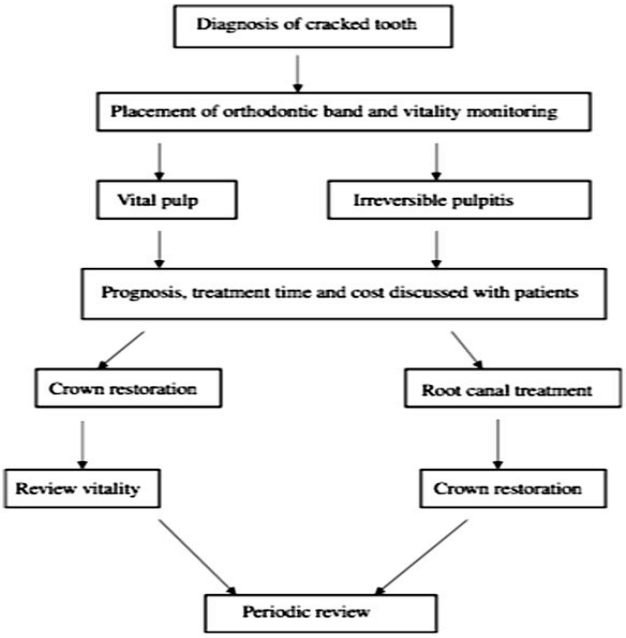
Bergstrom J 2004 (Journal of Oral Sciences): Tobacco smoking not associated with apical periodontitis

Krall et al 2006 suggested that Smokers are 1.7 times more likely to have a root canal. There is a statistical dose-response relationship between cigarette smoking and the risk of root canal treatment.

In a case-control retrospective study (Lopez, 2012 JOE), the relation between smoking and apical periodontitis was assessed. It was noticed that after adjusting for age, gender, number of teeth, endodontic status, quality of root filling, and diabetic status, tobacco **smoking is strongly associated with the presence of radiographically diagnosed periapical lesions.**

"**Sickle cell anemia (SCA)**, the most common genetic disorder worldwide, is a hemoglobinopathy transmitted as an autosomal recessive non–sex-linked disease, which is common among individuals of African descent. This disease is caused by a point mutation in the β-globin gene of normal hemoglobin (HbA) resulting in a modified hemoglobin (HbS). The diagnosis of SCA is used for the homozygous form of the disease when a person receives a gene for HbS from each parent. When the subject receives a single gene for HbS from just 1 parent and a gene for HbA from the other, he/she does not have the disease but is a carrier of the sickle cell trait" **(Silva Costa 2013, JOE).** It was shown that the **occurrence of PN in clinically intact permanent teeth was 8.33 times higher in the SCA group than in the normal group.**

Crack, VRF:



Always dry tooth to look for a crack. Transillumination, wedge, stain, biting test (pain on releasing or biting) can help to detect cracks. FORESHORTENING the tooth in radiographs after trauma makes it easier to diagnose a crack or a fracture.

Cameron JADA 1971 talked about cracked teeth syndrome. **Rivera** also discusses the cracked tooth, one of the five major classifications of longitudinal tooth fractures: **1) craze line; 2) cuspal fracture; 3) cracked tooth; 4) split tooth; and 5) vertical root fracture**

Common teeth to be cracked is mandibular second molar mesiodistally due to smaller occlusal table than 1st Usually teeth with a small or no filling (30%). Mandibular second molars have a higher incidence of vertical root fractures, followed by maxillary first molars and maxillary premolars.

In mandibular molar teeth with non intact lamina dura and necrosis without any carious or large restoration; suspect cracked tooth syndrome.

Berman & Kuttler 2010 JOE: Pulp necrosis in the absence of restorations, caries or luxation injuries is likely caused by a longitudinal fracture extending from the occlusal surface and into the pulp.

Deog-Gyu Seo (2012, JOE) Investigated the factors associated with cracked teeth. Upper first molar (28.0%) was most frequently cracked followed by the lower first molar (25.2%), the lower second molar (20.6%), and the upper second molar (16.8%). The prevalence of longitudinal tooth fractures found in a premolar was 6.6% and 2.8% in the maxilla and mandible, respectively. For the clinical signs and symptoms, 51% of the patients experienced bite pain, and 82.2% respond positively on the bite test. Sixty teeth (56.1%) were negative on the percussion test, whereas 36 teeth (33.6%) showed moderate to severe cold sensitivity.

Irene G.B. Sim (JOE, 2016): Multivariable analyses found that the presence of extension of cracks onto the pulpal floor increased the odds of tooth loss by 11-fold (odds ratio = 11; 95% CI, 1.2–97; P = .03) with other factors being held constant. The Kaplan-Meier plot of survival of teeth without and with extension of crack onto the pulpal floor is shown in Figure. The 5-year (60 months) survival estimate in the absence of extension of cracks onto the pulpal floor was 99% versus 88% in the presence of extension of cracks onto the pulpal floor.

Ferrari et al. showed that 10 to 12 years after endodontic treatment, there is progressive degradation of the demineralized collagen matrices. The aging dentin becomes sclerotic and exhibits very limited yielding before failure. The fracture toughness is lower, and the stress–strain response is characteristic of brittle behavior.

Zelik (Serbia- IEJ, Finite element analysis, 2015): Teeth with two-surface composite restorations that underwent root canal treatment are less resistant to high occlusal load, but the main contribution to their weakening arises from access cavity preparation. Canal enlargement does not contribute to this process substantially.

Rud, Omnel: VRF is hard to detect on x-rays. When a vertical root fracture is present, it is observed in a radiograph only 35.7% of time.

Dang & Walton (1989): The hand spreader (D11) cased more root distortion and vertical fx then the B finger spreaders. Therefore, **VRF is more common in endodontically treated teeth.**

Rundquist BD (2006) How does canal taper affect root stresses? With increasing taper, root stresses decreased during root filling but tended to increase for masticatory loading. Root fracture originating at the apical third is likely initiated during filling, while fracture originating in the cervical portion is likely caused by occlusal loads.

Bender: most common cause of vertical root fractures may be **iatrogenic dental treatment**. Dental procedures such as the placement of posts and pins or the tapping into place of a tightly fitting post or intracoronal restoration may induce a vertical root fracture. The most common dental procedure contributing to vertical root fractures is endodontic treatment.

Tamse, Fuss: Suggested the presence of J-shaped lesions in VRF. VRF is seen mostly in tooth with short and screwed posts. Mostly in maxillary second PM > Mandibular first molar > Maxillary central and lateral.

Tamse (2015, JOE): Two-canal mesial roots are much more prone to VRF than 1-canal distal roots. We suggest that VRF may occur during clinical condensation of gutta-percha in mesial roots of mandibular molars as well as other roots with canals connected by isthmus.

Pits and Natkins first talked about j shaped in VRF **Radiographic signs**: Actual separation of root fragments or fracture lines can be conclusive or suggestive evidence. If **radiopaque filling material extrudes** into a fracture line it may appear on an x-ray. A halo-like radiolucency, especially if it involves two opposite sides of a root are suggestive for fractures. Periodontal bone lesions **narrow, step-like in shape, angular in a**ppearance are suggestive of root fractures. Resorption along the fracture line and loosened retro-fillings suggest possible root fracture.
Clinical signs: At the time of root filling - sharp cracking or popping sounds maybe heard, the patient may feel a sharp stab of pain, pain with continued condensation and or bleeding into the canal, all which indicate a possible fracture. Narrow, rectangular periodontal pockets, essentially sinus tracts, have a characteristic feel when probed different from **crater-like defects** of chronic periodontitis and may suggest a vertical fracture. Visualization maybe possible if the gingiva can be retracted slightly or has receded. Dark staining or a clicking when explored may indicate a fracture line. Transillumination may help visualize. **Surgical exposure and use of dyes confirm a vertical fracture.**

Sings of VRF according to **Farber**: 1) The **repeated falling out of a coronal restoration** could be due to a fracture between the axial walls of the preparations; as the fractured segments flex or move apart, the restoration between these segments may lose its resistance form, become loose, and dislodge. Similarly, a retrograde restoration that has become dislodged could be secondary to a vertical root fracture apically.

2) **Multiple Sinus Tracts** Also indicative of a vertical root fracture is the presence of multiple sinus tracts adjacent to the tooth in question. Because the fracture may be present on at least two surfaces of the tooth, the infected area may drain to multiple sites, creating multiple sinus tracts.

Microleakage:

Vire JOE 1991: 59.4% cause of tooth loss is due to coronal microleakage!! 32% (1/3) due to periodontal disease (do periodontal examination before RCT) and 8.6% RCT problems which is mostly due to vertical root fracture from lateral obturation using spreader (Endo failures usually happen quickly in 2 years and perio 5 years).

Song et al 2011 JOE
493 teeth were analyzed for the cause of failure in root canals treatment done **under microscope** when examined under a microscope during endodontic microsurgery.
Cause for failures were:

- **30.4% leakage around the root filling material**
- **19.7% Missed canal**
- 14.2% Underfilling
- 8.7% anatomical complexity
- 3% Overfilling
- 2.8% Iatrogenic defects
- 1.8% apical calculus
- 1.2% cracks

Babacar Toure (JOE, 2011) in a prospective study investigated the reasons for extraction of endodontically treated teeth. Mandibular first molar with out crown was the most extracted tooth. **Periodontal disease (40.3%) was the most frequent**. Other reasons included endodontic treatment failure (19.3%), vertical root fracture (13.4%), nonrestorable cuspid and crown fracture (15.1 %), non-restorable caries 5.2%, iatrogenic perforations and stripping 4.2%, prosthetic 0.8%, and total crown destruction (1.7%).

Ray and Trope IEJ 1995: Main idea of this study is that a good coronal restoration determines the final outcome.

Good endo, Good crown 91.4% success rate
Bad endo, Good crown 67.6%
Good endo, Bad crown 44.1%
Bad endo, Bad crown 18.1%

A similar study was done by **Aline C. Gomes (JOE, 2015)** assessing the influence of endodontic treatment and coronal restoration on status of periapical tissues: **A Cone-beam Computed Tomographic** Study. The odds ratio allowed the conclusion that it is **0.6 times most probable to observe a healthy periapical condition when you have the presence of coronal restoration when compared with an absence of coronal restoration**. Regarding the apical extension of the filling, the best results were observed for canals filled within to 0–2 mm short of the apex, with a statistically significant difference over teeth with over- or underfilling. It is 4.68 times more likely to find healthy teeth when the apical extension of the filling is 0–2 mm short compared with teeth with overfilling. The apical extent of the filling >2 mm short from the foramen also displays an odds ratio of 2.024, which corresponds to a significantly higher possibility of finding healthy teeth compared with overfilling. The odds ratio shows that it is 2.5 times more probable to have periapical health when there are satisfactory periapical endodontic treatments than when this treatment is unsatisfactory. When there was adequate endodontic treatment and coronal restoration was present, it was categorized as healthy 59.44% of the time. This condition showed a significantly better outcome than the others did ($P < .0001$). Teeth with inadequate treatment and absent restoration yielded the highest prevalence of disease (77.14%).

Brian M. Gillen & Looney: Impact of the quality of coronal restoration versus the quality of root canal fillings on success of root canal treatment: **a systematic review and meta-analysis JOE (2011):** On the basis of the current best available evidence, the odds for healing of apical periodontitis increase with both adequate root canal treatment and adequate restorative treatment. Although poorer clinical outcomes may be expected with adequate root filling-inadequate coronal restoration and inadequate root filling-adequate coronal restoration, **there is no significant difference in the odds of healing between these two combinations.**

Influence of coronal restoration and root canal filling quality on periapical status: clinical and radiographic evaluation. Craveiro, Fontana (JOE 2015) Using either a radiographic or clinical assessment alone was not a reliable method to ascertain whether restoration quality could be correlated with postoperative periapical status. **Poor root canal filling quality was a prognostic determinant** of endodontic treatment failure, whereas coronal restoration quality had a lesser impact on the outcome of the endodontic treatment.

Cockren & Miller suggested use of rubber dam. Later **Po-Yen Lin (2014, JOE**) documented the importance of using rubber dam. The survival probability of initial RCT using rubber dams after 3.43 years (the mean observed time) was 90.3%, which was significantly greater than the 88.8% observed without the use of rubber dams. The use of a rubber dam during RCT could provide a significantly higher survival rate after initial RCT. **This result supports that rubber dam usage improves the outcomes of endodontic treatments.**

Classic coronal microleakage Studies:

Swanson & Madison (1987): Demonstrated that it **took only 3 days** for coronal leakage of a tracer dye to reach apex.

Madison & Wilcox (1988): Emphasized importance of coronal seal**. 3 day dye leakage.**

Magura (1991): Reported that it took **3 months** for bacterial coronal leakage to percolate through RCT filling. Suggest need to **re-tx** if RCT tooth is not restored within 3months.

Torabinejad (1990): Coronal microleakage with bacteria. **Motile** bacteria recontaminated obturated root canal systems in 49 days. **Non-motile** bacteria recontaminated obturated root canal systems in an average of 24 days.

Torabinejad, Ung and Kettering 1990: leakage of bacteria from unrestored root canal treated teeth starts from *1-4 days*. Motility of the organisms was not a factor.

Khayat & Torabinejad (1993): Demonstrated recontamination of obturated root canal systems when bacteria placed in natural saliva within 30 days. They showed that there is NSD between lateral and vertical obturation in the amount of micro leakage.

Alves (1998): Compared bacterial (Campylobacter rectus, Peptostreptococcus micros, Fusobacterium nucleatum, Prevotella intermedia) leakage of LC obturated canals with post-space prep to endodoxin. Endotoxin leaked faster than bugs (Means: 23 days vs 62 days)

Trope (1995): Endotoxin penetration of coronallly unsealed NSRCT teeth **<21 days**. Emphasizes importance of coronal seal

Based on bacterial and endotoxin leakage studies of Torabinejad, Khayat, Alves & Trope , you should consider re tx leaking NSRCT case if open > 3 weeks.

Saunders & Saunders (1990): Suggested place Vitrebond glass ionomer material over canal orifice and pulpal floor to minimize coronal microleakage.

Roghanizad (JOE)= talked about **intraorifice barrier** / 3 mm of the coronal gutta-percha was replaced by either Cavit, TERM, or amalgam with cavity varnish. After thermo cycling and 2 wk of immersion in dye, the amount of dye penetration was measured. **The results showed that amalgam with two coats of cavity varnish sealed significantly better than Cavit and TERM**. However, Cavit and TERM were still significantly better than a positive control group.

Study by **Balto et al.** found that all of the provisional materials they tested in post-prepared root canals failed to prevent coronal leakage when used for an average of 30 days. Similarly, **delayed placement of the definitive restoration had an impact on the prognosis of ETT.**

Weber: 3.5mm cavit would prevent micro leakage.

Wilderman (1971): Cavit is composed of Zinc oxide, calcium sulfate, glycol acetate, triethanolamine, polyvinyl acetate, polyvinylchloride acetate, red pigment. It is Hygroscopic.

Anderson sterilize & Powell (1988) Cavit and TERM provided better seal than IRM which is not significantly different from intact crowns. Also reported by **Barkhorder 1990.**

Teplitsky: Thermal variation does not affect the cavit ability to maintain seal.

Deveaux (1999): Bacterial leakage study (S. sanguis) Cavit better than TERM & IRM

Trauma, Vital pulp therapy, Regeneration and apexification:

MTA and **Brasseler Root Repair Material** contain **calcium silicates** which were shown to to promote cell differentiation, to have osteoconductive effects, and also to reduce inflammation of human dental pulp cells (hDPCs) **(Chen)**

Bergenholtz G. Micro-organisms from necrotic pulp of traumatized teeth. Odontol Revy 1974.
64% of the time, traumatized teeth with necrotic pulps have a mixed flora with anaerobes predominating. Trauma led to an aseptic necrosis in the other teeth.

Andreasen: 22% of traumatized teeth undergo calcific metamorphosis (Pulp canal obliteration). Only 8.5% developed pulp necrosis which need RCT.

Most common dental injuries in Primary dentition: Luxation; Permanent: Crown fracture (**Andreasen**)

Walton: Canal present histologically, although absent radiographically!!!

Andreasen 1972: There is always a persisting narrow pulp canal, even in calcified traumatic teeth.

Holcomb & Gregory: RCT if PARL develops; only 7% require RCT/ Holcomb= Calcific metamorphosis of the pulp: Its incidence and treatment if assymptomatic and no lesion in 75% cases don't touch the tooth / The only definite criterion for endodontic or surgical intervention in calcific metamorphosis appears to be the appearance of periapical rarefaction on the roentgenogram. / According to Andreason only 8.5% of cases following CM need RCT.

Anderson theorized that nervous control of blood flow to odontoblasts is altered following trauma, causing uncontrolled reparative dentin or hemorrhage and clot formation act as a nidus for calcification. Occurs mostly in immature teeth.

Cvek: Advocated partial pulpotomy (removing 1.5-2 mm pulp) even **72hr after traumatic exposure**. Remember that need remove blood clot (Schroder 1971). **Cvek pulpotomy = 96% healing 3-15 yr follow-up.**

The management of **permanent teeth with incomplete root development** with compromised pulpal integrity presents a unique challenge. The preservation of pulp vitality is of the utmost importance for continued dentin formation and root development in immature teeth. The loss of pulpal vitality before the completion of dentin deposition leaves a weak root more prone to fracture as a result of the thin dentinal walls. **Keswani (JOE, 2014)** compared the effectiveness of MTA and platlet rich fibrin in pulpotomy. In this clinical trial it was found that there is no significant difference between the 2 groups in terms of clinical and radiologic success. Radiographically, all available cases (53 teeth) showed evidence of root growth and canal narrowing. Complete apical closure was observed in 88.8% in the PRF group (experimental group) and 80.07% of roots in the MTA group (control group), respectively, at 24 months.

Holland: removal of debris is the most important phase of apexification treatment.

Frank (1966): Described apexification techniques with Ca(OH)2. Nonvital immature teeth treated with CaOH developed four different types of apical barrier formation. Was the 1st to describe technique. 4 repair types:
1- periapex closes with definite recession of the root canal.
2- obliterated apex develops without any change in canal space.
3- no radiographic evidence of development in canal or apex; an apical stop is evident clinically.
4- calcific bridge forms coronal to apex that is detectable radiographically.

Katebzadeh N, Dalton BC, Trope M. Strengthening immature teeth during and after apexification. J Endod 1998. Strengthen the cervical portion of immature teeth with composite during apexification to prevent fracture.

Cvek (1972): Tx necrotic teeth with incompletely formed apices with Ca(OH)2. **95%** success for apical closure.

Yates: If you replace the CaOH **early** you will have better result for apexification. The mean barrier formation time was **9 months. The presence of infection did not affect the barrier formation but the width of the open apex was a determinant factor.**

What materials can be use as apical barrier?

1) MTA: **Torabinejad** (use CaOH for 1 w befor MTA in the infected cases) **Andereason** suggested 4 mm MTA
2) CaOH: 2mm thickness for creating barrier suggested by **Weisenseel**
3) **Holland**: Use of dentinal shavings

Menta (JOE, 2013) assessed the outcome of the treatment of teeth with open apices managed by the orthograde placement of mineral trioxide aggregate (MTA) apical plugs. Of 252 examined teeth (88% recall rate), **90% were healed**. Teeth with and without preoperative periapical radiolucencies demonstrated healed rates of 85% and 96%, respectively. Orthograde placement of MTA apical plugs appears to be a promising treatment option for teeth with open apices. The presence of preoperative apical periodontitis was identified as an important prognostic factor. Also **Menta in 2014 (JOE)** compared the long term success of **direct pulp cap** using MTA versus CaOH. It was found that **MTA provides better long-term results after direct pulp capping compared with CH**. Placing a permanent restoration immediately after direct pulp capping is recommended.

Falk Schwendicke (JOE, 2014) compared the DPC and RCT following **carious exposure**. Despite requiring follow-up treatments significantly earlier, teeth treated by Direct Pulp Cap (DPC) were retained for long periods of time (52 years) at significantly reduced lifetime costs (545 vs 701 Euro) compared with teeth treated by RCT. For teeth with proximal instead of occlusal exposures or teeth in patients >50 years of age, this cost-effectiveness ranking was reversed. Although sensitivity analyses found substantial uncertainty regarding the effectiveness of both strategies, DPC was usually found to be less costly than RCT. **It was found both DPC and RCT suitable to treat exposed vital, nonsymptomatic pulps. DPC was more cost-effective in younger patients and for occlusal exposure sites, whereas RCT was more effective in older patients or teeth with proximal exposures.** These findings might change depending on the health care system and underlying literature-based probabilities.

Calcium hydroxide has been a material of choice for pulp capping since 1930 because of its antibacterial activity, ability to release calcium and hydroxyl ions, and low potential for irritation of the traumatized

pulp tissue and . However, it has major disadvantages including high solubility, dissolution in tissue fluids, and poor sealing ability (Nowicka, JOE

Zhaofei Li (2015, JOE, Meta analysis): Direct Pulp Capping with Calcium Hydroxide or Mineral Trioxide Aggregate: A Meta-analysis

- In clinical trials, mineral trioxide aggregate (MTA) showed a higher success rate than calcium hydroxide (CH).
- MTA resulted in less pulpal inflammatory response than CH.
- MTA was superior to CH in terms of dentin bridge formation.

Emad AlShwaimi (JOE, 2016) assessed the application of betamethasone/gentamicin (BG) cream as a pulp capping material. It was shown that MTA resulted in a significantly better pulpal response, with less inflammation and a thicker dentin bridge at 8 weeks.

Johannes Mente (JOE, 2010): Multiple analysis showed that teeth that were permanently restored ≥2 days after capping had a significantly worse prognosis in both groups. MTA appears to be more effective than calcium hydroxide for maintaining long-term pulp vitality after direct pulp capping. The immediate and definitive restoration of teeth after direct pulp capping should always be aimed for.

Tronstad (OOO, 1972): DPC of carious exposure had less than 50% success rate.

Alicja Nowicka reported that Biodentine had a similar efficacy in the clinical setting and may be considered an interesting alternative to MTA in pulp-capping treatment during vital pulp therapy.

René Gruythuysen (2010, JOE) in a retrospective survival analysis study estimated that survival rate was 96% for primary molars (mean survival time, 146 weeks) and 93% for permanent teeth (mean survival time, 178 weeks) following IPC, liner, GI and permanent restoration. This study shows that IPT performed in primary and permanent teeth of young patients may result in a high 3-year survival rate.

Regenerative Endodontic:

Please know the AAE Guide-line step by step word by word!!

<AAE Clinical Considerations for a Regenerative Procedure>

Case Selection: • Tooth with necrotic pulp and an immature apex. • Pulp space not needed for post/core, final restoration. • Compliant patient/parent. • Patients not allergic to medicaments and antibiotics necessary to complete procedure (ASA 1 or 2).

Informed Consent • Two (or more) appointments. • Use of antimicrobial(s). • Possible adverse effects: staining of crown/root, lack of response to treatment, pain/infection. • Alternatives: MTA apexification, no treatment, extraction (when deemed nonsalvageable). • Permission to enter information into AAE database (optional).

First Appointment • Local anesthesia, dental dam isolation and access. • Copious, gentle irrigation with 20ml NaOCl using an irrigation system that minimizes the possibility of extrusion of irrigants into the periapical space (e.g., needle with closed end and side-vents, or EndoVac™). Lower concentrations of NaOCl are advised [1.5% NaOCl (20mL/canal, 5 min) and then irrigated with saline or EDTA (20 mL/canal, 5 min), with irrigating needle positioned about 1 mm from root end, to minimize cytotoxicity to stem cells in the apical tissues. • Dry canals with paper points. • Place calcium hydroxide or low concentration of triple antibiotic paste. If the triple antibiotic paste is used: 1) consider sealing pulp chamber with a dentin bonding agent [to minimize risk of staining] and 2) mix 1:1:1 ciprofloxacin: metronidazole: minocycline to a final concentration of 0.1 mg/ml. • Deliver into canal system via syringe • If triple antibiotic is used, ensure that it remains below CEJ (minimize crown staining). • Seal with 3-4mm of a temporary restorative material such as Cavit™ , IRM™ , glassionomer or another temporary material. Dismiss patient for 1-4 weeks.

2 Second Appointment (1-4 weeks after 1st visit) • Assess response to initial treatment. If there are signs/symptoms of persistent infection, consider additional treatment time with antimicrobial, or alternative antimicrobial. • Anesthesia with 3% mepivacaine without vasoconstrictor, dental dam isolation. • Copious, gentle irrigation with 20ml of 17% EDTA. • Dry with paper points. • Create bleeding into canal system by over-instrumenting (endo file, endo explorer) (induce by rotating a pre-curved K-file at 2 mm past the apical foramen with the goal of having the entire canal filled with blood to the level of the cemento–enamel junction). An alternative to creating of a blood clot is the use of platelet-rich plasma (PRP), platelet rich fibrin (PRF) or autologous fibrin matrix (AFM). • Stop bleeding at a level that allows for 3-4 mm of restorative material. • Place a resorbable matrix such as CollaPlug™ , Collacote™ , CollaTape™ or other material over the blood clot if necessary and white MTA as capping material. • A 3–4 mm layer of glass ionomer (e.g. Fuji IX™ , GC America, Alsip, IL) is flowed gently over the capping material and light-cured for 40 s. MTA has been associated with discoloration. Alternatives to MTA (such as resin-modified glass ionomer [RMGI] or bioceramics [e.g., Biodentine®]) should be considered in teeth where there is an esthetic concern. o Anterior and Premolar teeth - Consider use of Collatape/Collaplug and restoring with 3mm of a nonstaining restorative material followed by bonding a filled composite to the beveled enamel margin. o Molar teeth or teeth with PFM crown - Consider use of Collatape/Collaplug and restoring with 3mm of MTA, followed by RMGI, composite or alloy.

Follow-up • Clinical and Radiographic exam o No pain, soft tissue swelling or sinus tract (often observed between first and second appointments). o Resolution of apical radiolucency (often observed 6-12 months after treatment) o Increased width of root walls (this is generally observed before apparent increase in root length and often occurs 12-24 months after treatment). o Increased root length. o Positive Pulp vitality test response • The degree of success of Regenerative Endodontic Procedures is largely measured by the extent to which it is possible to attain primary, secondary, and tertiary goals: o Primary goal: The elimination of symptoms and the evidence of bony healing. o Secondary goal: Increased root wall thickness and/or increased root length (desirable, but perhaps not essential) o Tertiary goal: Positive response to vitality.

Hargreaves compare three different methods of treating immature teeth (REVASCULARIZATION, MTA APEXIFICATION, CaOH APEXIFICATION) with pulp necrosis in a **retrospective study (JOE, 2015).** The percentage change of root width was significantly greater in the revascularization group (28.2%) compared with the MTA apexification (0.0%) and calcium hydroxide apexification groups (1.5%). In addition, the percentage increase of root length was significantly greater in the revascularization group (14.9%) compared with the MTA (6.1%) and calcium hydroxide apexification groups (0.4%). Moreover, the **survival rate of the**

revascularization-treated teeth (100%) and MTA apexification–treated teeth (95%) were greater than the survival rates observed in teeth treated with calcium hydroxide (77.2%).

Intracanal disinfection is a crucial step in regenerative endodontic procedures. However, this novel endodontic treatment lacks standardization. **Hargreaves (2011, JOE)** assessed the survival of stem cells from the apical papilla (SCAP) following different irrigation protocols. Irrigation with 17% EDTA best supported cell survival followed by irrigation with 6% NaOCl/17% EDTA/6% NaOCl. Conversely, protocols that included 2% CHX lacked any viable cells.

Recently **(Nozomu Yamauchi, 2011, JOE)** it has been shown that the use of cross-linked collagen scaffold and exposure of dentin matrix combined with blood clot might provide an efficient approach to generate a vital support structure for the treatment of immature teeth with apical periodontitis.

Histologic Characterization of Regenerated Tissues in Canal Space after the Revitalization/Revascularization Procedure of Immature Dog Teeth with Apical Periodontitis, Wang (JOE,2010): The canal dentinal walls were thickened by the apposition of newly generated cementum-like tissue termed herein "intracanal cementum (IC)." One case showed partial survival of pulp tissue juxtaposed with fibrous connective tissue that formed IC on canal dentin walls. The IC may also form a bridge at the apex, in the apical third or midthird of the canal. The root length in many cases was increased by the growth of cementum. The generation of apical cementum or IC may occur despite the presence of inflammatory infiltration at the apex or in the canal. These cementum or cementum-like tissues were similar to cellular cementum. Bone or bone-like tissue was observed in the canal space in many cases and is termed intracanal bone (IB). Connective tissue similar to periodontal ligament was also present in the canal space surrounding the IC and/or IB.

It is not surprising that the rate of root maturogenesis is variable because of unique individual circumstances. It may be that teeth with longstanding necrosis are more likely not to have remaining viable pulp tissue and perhaps diminished regenerative capacity. Indeed, a number of case reports indicate cases of traumatized incisor teeth where the regenerative procedure failed to result in further root maturogenesis. Therefore, the many case series reporting 100% success for regenerative procedures as tabled in **Torabinejad and Faras** may not reflect true outcomes for success because it is likely that unfavorable cases are not reported. In a prospective study by **Khalar (JOE, 2014)** the mean score for the presence of periapical radiolucency in the postoperative image was 9.7%. Apical closure after treatment was assessed as incomplete in 47.2%, and complete apical closure was recorded in 19.4% of cases.

Nagata (JOE, 2014) compared the long term effectiveness of two different revascularion method 1) Using Tri antibiotic past 2) CaoH as intracanal medicament. Revascularization outcomes for traumatized patients treated with the tested protocols presented **similar** clinical and radiographic data. However, TAP caused esthetic problem leading to tooth discoloration, which can be considered a disadvantage when compared with CaOH. Also another issue was addressed by **Berkhoff (JOE, 2014)** who showed that Current irrigation techniques do not effectively remove TAP from root canal systems, possibly because of its penetration and binding into dentin. However, calcium hydroxide is effectively removed with significant less residual presence.

In regenerative endodontics, it is believed that EDTA induces odontoblast differentiation by releasing growth factors from the dentin matrix. **Nan-Sim Pang (JOE, 2014)** assessed the effectiveness of **EDTA** on differentiation of dental pulp cell. Results showed that EDTA induced cell attachment and odontoblastic/osteoblastic differentiation, which was observed only in the group in which the DPSCs were

placed in direct contact with the EDTA-treated dentin surfaces. These findings suggest that EDTA is beneficial for achieving successful outcomes in regenerative endodontics.

Current research is concerned with discovering better scaffolds for use in regenerative endodontic treatment. platelet-rich plasma (PRP) has been suggested by some articles as a superior alternative for Blood clot. **Bezgin (JOE, 2015)** stated that PRP successfully created a scaffold for regenerative endodontic treatment; however, treatment outcomes did not differ significantly between PRP and conventional BC scaffold.

Internal inflammatory root resorption destroys dental hard tissue by odontoclast activity and **Internal resorption** starts inside the root canal and **requires at least partially vital pulp tissue**. If the resorption is not detected and remains untreated, it can potentially grow larger and eventually perforate the root from inside. When internal resorption is detected early enough, the treatment is usually successful, and the long-term prognosis of the affected tooth is good. **In 2012 Happasalo (JOE)** study the prevalence of Internal resorption was estimated. He suggested that tooth vital normal pulp don't go under inflammatory resorption. While it is more common in teeth with pulpitis or necrosis. It is more common in middle third of the root.

Gartner & Mack: (1976 JOE): Classic: Diff dx of Int vs Ext: **Internal**: sharp margins, canal not observed inside lesion, symmetrical, uniform density, doesn't move on shift shot, less common, more predictable, tx=CaOH +RCT. **External**: irregular margins, can see canal thru lesion, asymmetrical, variable radiodensity, moves on shift shot, more common, less predictable, tx= depends.

Trope Also Fuss confirmed the same finding= In order for root resorption to happen two things must occur 1) **Loss of protective layer** (precementum and predentin) and 2) **inflammation must occur**. It has been suggested that osteoclast just bind to RGD peptides that bound to calcium salt of mineralized surface. Therefore, presence of predentin which is un mineralized prevent activation of dentinoclast.

Turkun (Endod Dent Trauma 1997) = Conventional RCT is treatment choice for non-perforating internal resorption. In perforating remineralization treatment with CaOH is indicated but surgery may be needed. The **success rate for non perforating case is 90% with 1 w CaOH** and warm condensation. 25% with perforating.

Trope suggested that **long term treatment with CaOH (12W)** is more effective than 1 W in treatment of established inflammatory root resorption (External).

Mattison (1984, JOE): There is NSD in the external root resorption between RCT treated tooth and vital teeth when subjected to ortho force.

Tronstad (1988 EDT): Internal resorption is maintained by RC infection coronal to site of the lesion
External root resorption caused by: trauma, periradicular inflammation, ortho, bleaching. Classified resorption as transient inflammatory (surface), internal, external (cervical, progressive external and replacement).

Silva, J. F. C. (IEJ, 2015): While timing of pulpectomy and patient's age at the moment of trauma were confirmed as important risk factors, **Single nucleotide polymorphisms** within the IL1 gene cluster did not affect the susceptibility for Inflammatory external root resorption after replantation of permanent teeth.

Type of injury determine the rate of pulp necrosis. Highest is intrusion and mature apex.

Infraction: incomplete fracture of enamel with no loss of tooth structure. No tenderness, no finding in radio, no need to follow up otherwise associated with luxation, 6-8 w follow

Enamel fracture: loss of tooth structure, no pulp exposure, sensitive to cold, no tendet to percussion, no mobility, bonding, 6-8 weeks follow up.

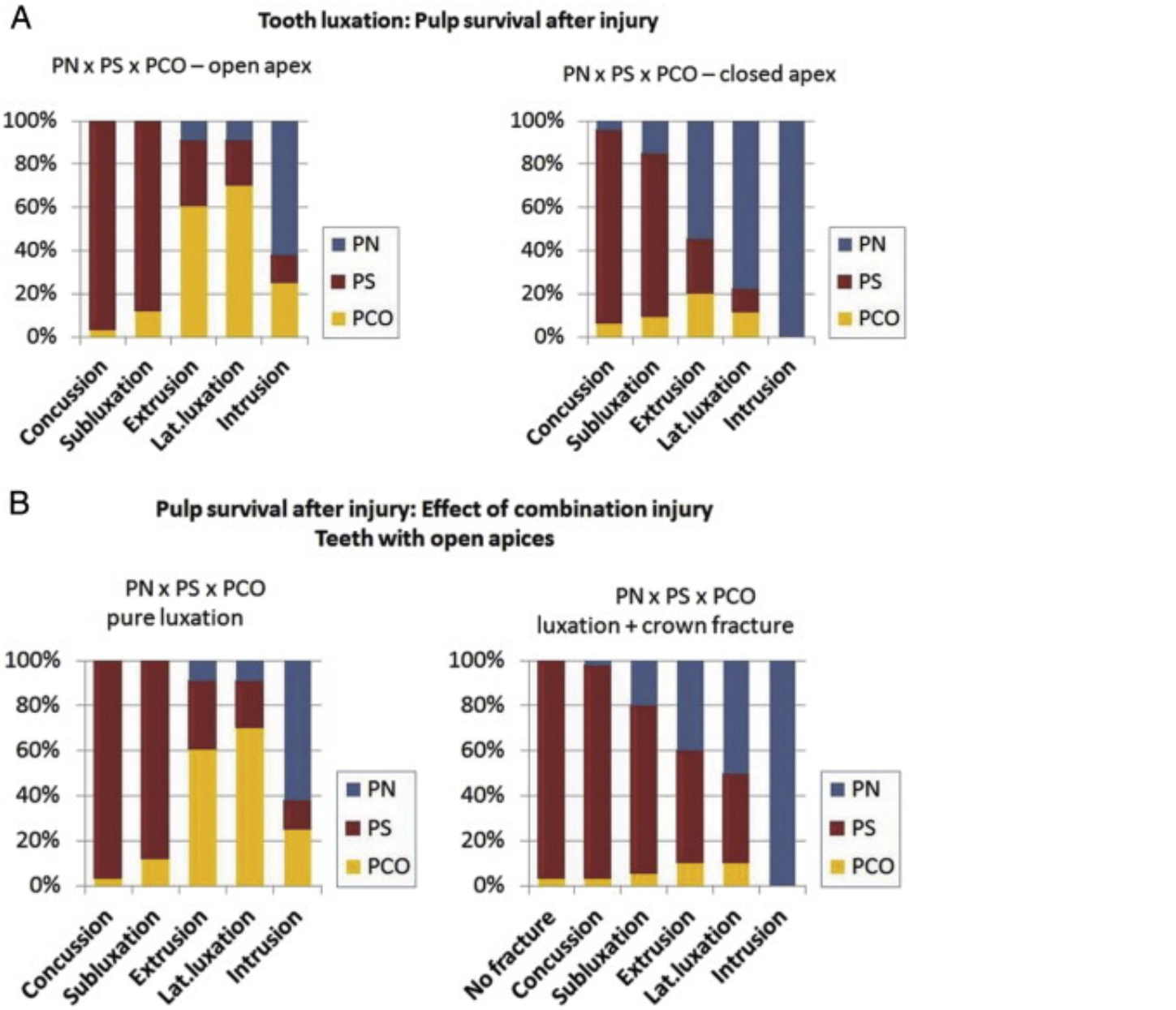
Enamel-dentin fracture: normal mobility, sensitivity, no percussion, use liner like biodentin, Brasslerr, MTA

Enamel, dentin, pulp fracture: In patients with immature apex try vital pulp therapy DPC or pulpotomy. In mature RCT, 6-8 w up to 1 y follow.

Crown-root fracture with pulp exposure: fragment removal, RCT or vital pulp therapy

Lateral extrusion, tooth displaced lab or lin: **Metallic sound percussion**, vitality depends on the severity (displacement of tooth from its original position with out avoultion)

Relationship between PN, PCO, and PS according to luxation injury and stage of root development (Andreasen JOE, 2015)



PN: Necrosis, PS: survival without any change, PCO: Pulp canal obliteration. From Andreasen FM, Pedersen BV. Prognosis of luxated permanent teeth: the development of pulp necrosis. Endod Dent Traumatol 1985;1:207–20. *B*, From Robertson A, Andreasen FM, Andreasen JO, Noren JG. Long-term prognosis of crown-fractured permanent incisors: the effect of stage of root development and associated luxation injury. Int J Paediatr Dent 2000;10:191–9.

The risk of PN increased with the extent of injury (ie, concussion < subluxation < extrusion < lateral luxation < intrusion). Moreover, teeth with completed root formation had a greater risk of PN than teeth with incomplete root formation. No treatment effect could be demonstrated. Humphrey et al found significantly decreased pulp survival with >6-mm intrusion compared with <3-mm intrusion in a study of 31 intruded incisors. In a study of 60 intruded permanent incisors, significant correlations with stage of root development and degree of intrusion (0–3 mm vs >7 mm) were found by **Tsilingaridis et al.**

By using multivariate regression statistics, **Lauridsen et al** found in combined luxation–crown fracture injuries that beside the already known variables for predicting PN after luxation injuries (ie, luxation diagnosis and stage of root development), **reaction to electrical pulp testing (EPT) at the time of injury played an important role. Thus, teeth that did not respond to EPT had a significantly greater risk of developing PN in the first year after injury.**

What is the probability of pulp necrosis following luxation injuries?
Andreasen: Concussion 4% (0% in immature teeth) ; Subluxation 15%; (0%) Extrusion 55% (9%); Lateral Luxation 77% (9%); Intrusion 100% (62%)

Best follow up for traumatic cases are **up to 6 months** due to **Ravn in Scan J Den Res** who showed that most changes occur in the first 6 months.

Kratchman S. Intentional replantation. Dent Clin North Am 1997. Best review of this procedure. Success rates of 80-85% should be seen: 1. It used to be advocated always to curettage the socket after removing the tooth. Now clinicians know not to touch the walls of the socket and only to aspirate gently the apical region if needed. 2. After removal, the tooth used to be held in gauze, desiccating viable PDL cells. Now the tooth is kept bathed in an emesis basin filled with HBSS, which maintains the viability of the PDL for 30 minutes. 3. All clinicians were able to do was visual inspection; now the microscope is used to illuminate and magnify the working area. 4. Splinting was done on every case; now clinicians rarely splint after replantation. 5. Narcotic pain medication was prescribed routinely; now clinicians premedicate with chlorhexidine rinse, anti-inflammatory medication, and sometimes antibiotics, rarely using narcotics. With increased understanding of the periodontium and improved techniques, replantation should no longer be viewed as a treatment of last resort, but rather a successful treatment alternative.

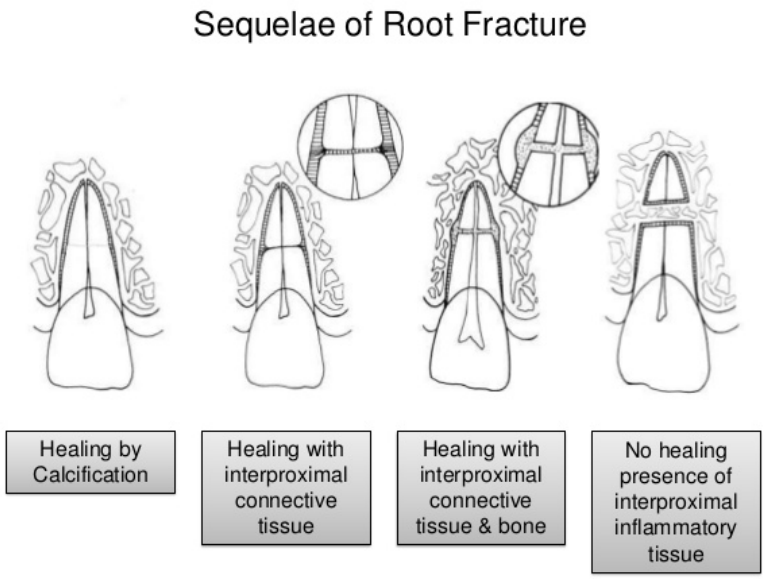
Management of dental traumas (Tables from Dr. Krell's study guide):

Uncomplicated crown fracture	❑ Baseline pulp test ❑ Smooth edges or restore with composite ❑ Place Dycal base on exposed dentin ❑ F/U at 2mos
Complicated crown fracture	❑ DPC if small, <24 hours, and open apex (dry CaOH2 on exposure, then Dycal, then restore) ❑ Cvek pulpotomy if larger, >24 hours, or closed apex (remove 2mm of pulp with diamond and H2O spray, then DPC). ❑ Pulpectomy if necrotic, uncontrolled hemorrhage ❑ F/U at 3, 6, 12mos, then annually
Crown-root fracture	4 options after removing coronal fragment: ❑ Gingival reattachment ❑ Crown lengthening ❑ Ortho extrusion ❑ Extraction

Cvek M, Andreasen JO. Pulp reactions to exposure after experimental crown fractures or grinding in adult monkeys. J Endod 1982 : Investigated the depth of inflammatory reactions of adult monkey pulps exposed by fracture or cavity prep at different times. Inflammatory changes in the pulp exposed by cavity preparation were 3.8 mm at 48 hr, 4.4 mm at 168 hour; increased in comparison to those in crown-fractured teeth (1.8 mm at 48 hr, 1.6 mm at 168 hr). **In crown-fractured teeth with vital pulp exposures up to a period of 7 days, not more than 2 mm of pulp beneath exposure needs to be removed.**

Root fracture	❑ 3 radiograph angles ❑ Reposition ❑ Rigid splint 2-4 months ❑ Adjust occlusion ❑ F/U at 3, 6, 12mos, then annually ❑ RCT of coronal segment if necrosis, apical matrix may be needed ❑ SX removal of apical segment if possible or necessary

Andreasen JO, Hjorting-Hansen E. Intraalveolar root fractures: radiographic and histologic study of 50 cases. J Oral Surg 1967: Described 4 types of healing following root fracture: calcified (callous), connective tissue, bone/connect tissue, granulation/inflammatory (nonunion). Location of fx did not determine success. Mobility of coronal segment is important (following figure form www.arefai.edublogs.org)



Bender IB, Freedland JB. Adult root fracture. J Am Dent Assoc 1983: Recommended 3 radiographs with different vertical angulations to view horizontal fracture. **Apical = better prognosis**.

Cvek M, Andreasen J, Borum M. Healing of 208 intraalveolar root fractures in patients aged 7-17 years. Dent Traumatol 2001: A positive effect of splinting (various methods) could not be demonstrated. In conclusion, the findings from this study have **cast doubts on the efficacy of splinting for root fracture** healing; hard tissue consolidation of a root fracture may take place more advantageously under functional stress.

Lateral Luxation	❑ Reposition and physiologic splint for 2-3 weeks ❑ Adjust occlusion ❑ Complete RCT if no response to vitality test in 3 weeks in closed apex ❑ Frequent F/U in open apex to R/O necrosis
Extrusion	❑ Same as lateral
Intrusion	❑ Open apex: loosen tooth with forceps, then allow to spontaneously reerupt, intervene with ortho if needed ❑ Closed apex: ortho repositioning is preferred ❑ Repositioning should be completed by 3 weeks ❑ RCT at 3 weeks

Trope (Pathways of the Pulp): If vitality testing indicates necrosis at the **3wk follow-up**, RCT should be performed due to high success of RCT in noninfected pulp versus risk of external root resorption complication.

Bhaskar SN, Rappaport HM. Dental vitality tests and pulp status. J Am Dent Assoc 1973.
EPT/cold/heat testing are unreliable following trauma. Trauma may damage nerve supply without altering blood supply. Vitality tests give information about pulpal nerve status only and **do not evaluate pulpal blood supply.**

Storage media for avulsed teeth:

Andreasen JO, Schwartz O. The effect of saline storage before replantation upon dry damage of the periodontal ligament. Endod Dent Traumatol 1986: Saline storage of a previously dry tooth has no effect on resorption or pulpal repair. A delay in replantation is acceptable if the teeth are placed in saline.

Andersson L, Hedstrom KG: Storage of experimentally avulsed teeth in milk prior to replantation. J Dent Res 1983. Milk is recommended as a storage medium in cases when immediate replantation is not possible. It has physiologic osmolality (280) and few bacteria. Teeth stored up to 6h in milk had same resorption as those immediately replanted. Saliva allows storage for up to 2h.

Hiltz J, Trope M. Vitality of human lip fibroblasts in milk, Hanks balanced salt solution and Viaspan storage media. Endod Dent Traumatol 1991.
Percentage of vital cells with milk: 68% at 6 hours, 43% at 12 hours, <1% at 48 hours.
Percentage of vital cells with H.B.S.S.: 71% at 24 hours, 38% at 48 hours, 0 at 120 hours.

Splinting	❑ Irrigate, aspirate above socket ❑ Physiologic splint, acid-etch resin/monofilament ❑ 7-10 days ❑ Use blunt instrument to reposition bone if collapsed

Andersson L, Lindskog S, Blomlof L, Hedstrom KG, Hammarstrom L. Effect of masticatory stimulation on dentoalveolar ankylosis after experimental tooth replantation. Endod Dent Traumatol 1985.
Hard diet vs. soft diet post replantation. Hard diet had less ankylosis.

After replantation, external root resorption (ERR) is a possible serious outcome that commonly results in tooth loss. In advanced stages of the inflammatory and replacement progressive forms of ERR, the weakened root walls become unable to endure even functional forces, thereby leading to the exfoliation of the tooth or to cervical root fracture. Replacement ERR (RERR) is related to the absence of vital periodontal ligament (PL) cells in the root surface, which results in tooth fusion to the alveolar bone. The damaged PL is repopulated by the adjacent bone marrow cells, followed by gradual replacement of the tooth structure by bone, a progressive condition that may lead to tooth loss because there is no effective treatment. **Juliana Vilela Bastos (JOE, 2014)** investigated the factors that are associated with occurrence and extent of ERR. **The patient's age at the moment of trauma had a marked effect on the ERR prevalence and extension. The patients older than 16 years at the moment of trauma had less chance of developing IERR and RERR (77% and 87%, respectively) before the pulp extirpation, regardless of the extension of the resorption**. The patients older than 11 years of age at the moment of trauma showed the lowest indices of IERR ($P = .02$). **Each day that elapsed between the replantation and the pulp extirpation increased the risk of developing IERR and RERR by 1.2% and 1.1%, respectively, and also raised the risk of severe IERR by 0.5% per day.**

How would you manage an avulsed tooth clinically?

- **From Pathways, Trope**

Management at site	❑ Gently wash if dirty, replant ❑ If unable to replant, store in: HBSS, milk, saline, saliva ❑ Proceed to office	**Andreasen JO. Effect of extra-alveolar period and storage media upon periodontal and pulpal healing after replantation of mature permanent incisors in monkeys. Int J Oral Surg 1981.** A significant relationship was found between the frequency of root resorption, extra-alveolar period and storage medium. This was especially evident after dry storage. Inflammatory resorption was common after dry storage and was related to the length of the extra-alveolar period. After 30 min dry storage, this resorption was very prominent.
Avulsion open apex <1 hour dry	❑ Rational: attempt to promote revitalization ❑ Soak 5 min in a suspension of 1 mg doxycycline in 20 ml physiologic saline ❑ HBSS rinse, replant ❑ Physiologic splint 7-10d ❑ Recall every 3 weeks for up to 18mos to monitor for root formation or necrosis ❑ If necrotic, proceed with apexification	**Cvek M, Cleaton-Jones P, Austin J, Lownie J, Kling M, Fatti P. Effect of topical application of doxycycline on pulp revascularization and periodontal healing in reimplanted monkey incisors. Endod Dent Traumatol 1990.** Topical application of doxycycline increased the frequency of pulp revascularization and decreased the frequency of microorganisms in the pulpal lumen. The frequencies of ankylosis and inflammatory root resorption were also decreased. Soak 5 min in a suspension of 1 mg doxycycline in 20 ml physiologic saline. **Kling M, Cvek M, Mejare I. Rate and predictability of pulp revascularization in therapeutically reimplanted permanent incisors. Endod Dent Traumatol 1986.** Frequency of revascularization in replanted teeth with apices >1mm diameter was 18% (increased to 33% at 4mm). No revascularization occurred when apical foramen <1mm. Less revascularization when replanted in >45min.
Avulsion open apex >1 hour dry	❑ Poor prognosis for revascularizing, consider alternate TX ❑ Rational if replanting: PDL is dead, prepare root to resist resorption ❑ Remove tissue tags with scaler ❑ Soak in 2% stannous fluoride for 5min ❑ Complete RCT extraorally, due to open apex, no time constraint (PDL is dead) ❑ Physiologic splint 7-10d	**Bjorvatn K, Selvig KA, Klinge B. Effect of tetracycline and SnF2 on root resorption in replanted incisors in dogs. Scand J Dent Res 1989.** Soaking in SnF2 will delay remodeling of the root into bone (replacement resorption). **Coccia CT. A clinical investigation of root resorption rates in reimplanted young permanent incisors: a five-year study. J Endod 1980.** Treatment of the root with Fl before replanting makes it osteoclast resistant, delaying replacement resorption. Twice the survival time can be expected. Trope, Pathways (5min 2% soak, immediate RCT)
Avulsion partially-fully closed apex <1 hour dry	❑ Rinse with HBSS, replant ❑ Physiologic splint 7-10days ❑ Clean and shape canal at 7d, remove splint, (rational: prevent infection of canal that leads to inflam resorp) Canal should not be infected to warrant 6mos dressing; place CaOH2 for 7-10d ❑ Obturate the canal at 7-10d	**Dumsha T, Hovland EJ. Evaluation of long-term calcium hydroxide treatment in avulsed teeth-- an in vivo study. Int Endod J 1995.** No differences in inflammatory resorption between avulsed teeth obturated with gutta percha or long term (5mos) calcium hydroxide. Perform RCT at 14-28 days and obturate with gutta-percha. **Trope M, Yesilsoy C, Koren L, Moshonov J, Friedman S. Effect of different endodontic treatment protocols on periodontal repair and root resorption of replanted dog teeth. J Endod 1992.** Short-(1wk) and long-term (8wk) calcium hydroxide treatment resulted in similar healing patterns when endodontic treatment is initiated 14 days after replantation of teeth.
Avulsion partially-	❑ Rational: PDL is dead, prepare root to	**Bjorvatn K, Selvig KA, Klinge B. Effect of**

fully closed apex >1 hour dry	resist resorption ❑ Remove tissue tags with scaler ❑ Soak in 2% stannous fluoride for 5min ❑ Physiologic splint 7-10days ❑ Clean and shape canal at 7d, remove splint, (rational: prevent infection of canal that leads to inflam resorp) Canal should not be infected to warrant 6mos dressing; place CaOH2 for 7-10d ❑ Obturate the canal at 7-10d	**tetracycline and SnF2 on root resorption in replanted incisors in dogs. Scand J Dent Res 1989.** Soaking in SnF2 will delay remodeling of the root into bone (replacement resorption). **Coccia CT. A clinical investigation of root resorption rates in reimplanted young permanent incisors: a five-year study. J Endod 1980.** Treatment of the root with Fl before replanting makes it osteoclast resistant, delaying replacement resorption. Twice the survival time can be expected. **Dumsha T, Hovland EJ. Evaluation of long-term calcium hydroxide treatment in avulsed teeth-- an in vivo study. Int Endod J 1995.** No differences in inflammatory resorption between avulsed teeth obturated with gutta percha or long term (5mos) calcium hydroxide. Perform RCT at 14-28 days and obturate with gutta-percha. **Trope M, Yesilsoy C, Koren L, Moshonov J, Friedman S. Effect of different endodontic treatment protocols on periodontal repair and root resorption of replanted dog teeth. J Endod 1992.** Short-(1wk) and long-term (8wk) calcium hydroxide treatment resulted in similar healing patterns when endodontic treatment is initiated 14 days after replantation of teeth. Trope, Pathways (5min 2% soak, immediate RCT)
Adjuncts	❑ Tetanus booster ❑ Chlorhexidine ❑ Analgesics ❑ Recall for 5 years	

Tooth autotransplantation is a treatment option that has the potential to restore masticatory function and esthetics to edentulous spaces resulting from extracted teeth by repositioning the patient's own teeth to another recipient site in the same patient. **Youngjune Jang (2016, JOE)** assessed the prognostic factors and clinical outcomes for autotransplanted teeth with complete root formation. It was concluded that the cumulative tooth survival rate was 68.2% at 12 years after the tooth autotransplantation. According to the Cox proportional hazard regression analysis, patient age, donor position, and extraoral time were significantly associated with tooth survival ($P < .05$). Donor extraction type was significantly associated with IRR ($P < .05$), and transplantation timing and initial stability were significantly associated with ankylosis ($P < .05$).

Irrigation and Medicament:

The main goals of irrigation: Debridement the canal; Dissolve tissue; Remove smear layer; Kill microbes ⇒fulfill biological principle of schilder's

Actually, antibacterial effectiveness of chemomechanical preparation is not apparently influenced by the number of instruments used; rather than that, significant elimination of bacterial populations has been shown to be influenced by the type, volume, concentration (Siqueira), and exposure time (DU, Shabahang= The most effective irrigation regimen was 5.25% at 40 minutes, whereas irrigation with 1.3% and 2.5% NaOCl for this same time interval was ineffective in removing E. faecalis from infected dentin cylinders. **) of the irrigant solution**

EDTA: Remove smear layer (inorganic), no disinfectant, can be used with bleach, no tissue dissolution
CHX: doesn't remove smear layer, antibacterial against planktonic, no tissue dissolution, can not be used with bleach
Naocl: Tissue dissolution, antibacterial, remove organic compartment, doesn't remove smear layer
QMIX: Disinfectant, Remove smear layer, can be used as a final irrigation (Haapasal, Franklin Tay)

Files shape; irrigants clean

If we compare the apical size preparation between classic and current literature, we can notice a significant decrease in the recommended size of apical preparation for effective irrigation. Also there are more emphasis on taper size in current literature for effective irrigation. Based on current literature it might be conclude that "overall taper and shape can compensate for the small apical size" (Matthew Brunson)

Ram (1977 OOO): Effective irrigation requires apical preparation. **Rec prep size of #40** to get effective delivery of irrigants. The irrigants can only progress 1mm beyond the tip of the needle

Khademi recommended prep size of min **#30** to get effective delivery of irrigants.

Hans Raj Saini (2012-JOE): The apical enlargement of the canal **3 sizes larger than the first apical biding file** is adequate, and further enlargement did not provide any additional benefit during endodontic treatment.

Andre Mickel: During crown-down preparation, the first crown-down file to reach the apex during instrumentation was noted (CDF). Teeth were then divided into three master apical file size groups of CDF 1, CDF 2, and CDF 3. There was a significant increase in the number of samples with negative cultures from CDF 1 to CDF 3. SEM observation revealed bacteria on dentinal walls and in tubules even in most negative canal cultures.

lynn Albrecht (JOE, 2004): evaluation of apical debris removal using various size and taper of profile: In conclusion, the results of this investigation suggest that debris is more effectively removed using .04, .06, and .08 ProFile GT instruments when the apical preparation size is larger (size 40) compared with size 20 apical preparations. When a taper of .10 can be produced at the apical extent of the canal, there is no difference in

debris removal between the two preparations sizes. This may be because of increased penetration of the irrigation needle and subsequent improvement in the effectiveness of irrigation. **They conclude that overall taper and shape can compensate for the small apical size.**

Matthew Brunson (JOE, 2010): Effect of Apical Preparation Size and Preparation Taper on Irrigant Volume Delivered by Using Negative Pressure Irrigation System. The data demonstrated that an increase in apical preparation size and taper resulted in a statistically significant increase in the volume of irrigant. In addition, an apical enlargement to ISO #40 with a 0.04 taper will allow for tooth structure preservation and maximum volume of irrigation at the apical third when using the apical negative pressure irrigation system.

L.G. Coldero (IEJ, 2002) evaluated the intracanal bacterial reduction using nickel-titanium rotary instruments with and without apical enlargement. It was speculated that there might be no significant difference in intracanal bacterial reduction when Ni-Ti GT rotary preparation with NaOCl and EDTA irrigation was used with or without apical enlargement preparation technique. It may therefore not be necessary to remove dentine in the apical part of the root canal when a suitable coronal taper is achieved to allow satisfactory irrigation of the root canal system with antimicrobial agents.

Nogueira Leal Silva (2013, JOE) performed randomized clinical trial on the effect of apical enlargement on the post operative pain. The foraminal enlargement and nonenlargement techniques resulted in the same postoperative pain and necessity for analgesic medication. This may suggest that the use of foraminal enlargement should be performed for endodontic treatment without increasing postoperative pain.

Salzgeber & Brilliant (1977): Irrigant reaches apex when canal systems are opened to file size 30

Abou-Rass (1982): The closer the needle is to the apex, the better the irrigation (ie, needle does not irrigate much past the bevel tip)

Dalton & Trope: Saw progressive **decrease in CFUs** with progressive sampling during filing with **larger files,** regardless of NiTi or SS. **Suggests that tx approach to infected teeth with AP may require additional antimicrobial measures than just instrumentation, irrigation and aseptic technique (ie, inter-appt Ca(OH)2).**

Boutsioukis (JOE, 2010) discussed the effect of needle insertion depth on irrigation pattern. Irrigant replacement reached the WL **only when the side-vented needle was placed at 1 mm**; therefore, it seems reasonable to suggest that this needle should be positioned within 1 mm from the WL if possible. Additional safety against irrigant extrusion in case of binding in the root canal is provided by the blind end of the side-vented needle. On the other hand, the flat needle and probably also similar types like the notched or the beveled needle should not be placed at 1 mm because of the high apical pressure developed. This pressure is likely to be even higher when the root canal is smaller and no safety feature like a blind-end needle is available to prevent forceful extrusion in case of binding. **The further the needle is positioned away from the WL, the less apical pressure is developed, but then the irrigant exchange is also less efficient and wall shear stress is lower. A reasonable compromise would be the 2- or 3-mm position, which still ensures adequate irrigant exchange.**

NaOCl: tissue dissolution, stop bleeding, lubricant, champagne effect for an extra canal, remove organic smear layer

Coolidge 1919 was the first to introduce NaOCL sodium hypochlorite. **Daiken:** Daiken Solution: WW1
Walker 1936: introduction of sodium hypochlorite as a root canal irrigant

Hand and Smith: 5.25% NaOCL has superior tissue dissolving properties. **Harrison and Hand:** Diluting NaOCL can reduce its effectiveness

Markus Haapasalo (JOE, 2010): Dissolution of the tissue increased almost linearly with the concentration of sodium hypochlorite. Higher temperatures and agitation considerably enhanced the efficacy of sodium hypochlorite. The effect of agitation on tissue dissolution was greater than that of temperature; continuous agitation resulted in the fastest tissue dissolution.

Bystrom A, Sundqvist G. Int Endod J 1985: NaOCl has superior antimicrobial effect to saline. No difference was noted between antibacterial effect of 0.5% and 5% NaOCl. The combined use of EDTA/NaOCl was more efficient, but did not eliminate all the bacteria. Bacteria that survive the instrumentation and irrigation rapidly increased in numbers between appointments.

Cvek and Lundberg 1983: found that increasing the concentration of sodium hypochlorite from 0.5% to 5% had little effect on the bactericidal efficiency.

Cvek: Antimicrobial effect of root canal debridement in teeth with immature root. A clinical and microbiologic study. 1976 : After the length has been confirmed radiographically, depending on the thickness of the remaining dentinal walls either a very light filing or no filing is performed with copious irrigation with **0.5%** sodium hypochlorite. A lower strength of sodium hypochlorite is used because of the danger of placing it through the apex of immature teeth. **The lower strength of sodium hypochlorite is compensated by the volume of the irrigant used**

Mahmoud Torabinejad (JOE, 2010): The most effective irrigation regimen was 5.25% at 40 minutes, whereas irrigation with 1.3% and 2.5% NaOCl for this same time interval was ineffective in removing *E. faecalis* from infected dentin cylinders. **High concentration and long exposure to NaOCl are needed for elimination of E. *faecalis* contaminated dentin.**

Baumgartner: NaOCl can't remove the smear layer. **Alternating EDTA and NaOCl** effectively removes smear layer, tissue, predentin and increases antimicrobial activity.

Baumgartner (JOE-2010) Compared apical extrusion of NaOCl Using the EndoVac or Needle Irrigation of Root Canals. This study showed significantly less extrusion risk using the EndoVac system compared with needle irrigation.

Baumgartner: **5.25% NaOCl** is safe for clinical use and does not increase postop pain

Hongyan Liu in 2010 (JOE) investigated the biofilm formation of E.faecalis and its susceptibility to Sodium Hypochlorite: Scanning electron microscopy and biofilm assay showed that starved cells were able to form biofilm on dentin with reduced efficiency as compared with the cells in the exponential phase and stationary phase ($p < 0.05$). Biofilm grown on dentin harbored more cells than polystyrene ($p < 0.05$). **Biofilms of starved cells were more resistant to 5.25% NaClO than those of stationary cells ($p < 0.05$), and the impact of 5.25%NaClO on them decreased as the biofilm matured.**

Rossi-Fedele (JOE, 2012) investigated the interaction of different common irrigations. The degradation and consequent deactivation of EDTA after its interaction with NaOCl is extremely slow, and, therefore, it does not compromise its clinical performance with respect to its chelating, smear layer removal, and dentin softening effects. However, in the presence of EDTA and chelating agents a dramatic reduction of FAC (free available chlorin) in NaOCl mixtures caused by chemical interactions appears to explain the inability of NaOCl and EDTA mixtures to dissolve soft tissues.

Haapasalo (JOE, 2010) showed the penetration of Naocl into the dentinal tobules. He showed that increasing the concentration (6%) and contact time (20 min) can increase the penetration depth to maximum (300 μ m)

Chlorine, which is responsible for the dissolving and antibacterial capacity of NaOCl, is unstable and consumed rapidly during the first phase of tissue dissolution**, probably within 2 minutes. Continuous replenishment** of the irrigant is essential

Siqueira (1998 EDT): 5% NaOCl destroyed Bacillus subtilis spores from GP cones within 1 min of immersion

Cunningham: Effect of temperature on collagen-dissolving ability of sodium hypochlorite endodontic irrigant. The 2.6% sodium hypochlorite solution at a temperature of 37 degrees C. was found to be equally effective as a collagen-dissolving agent when compared to 5.2% sodium hypochlorite at either 21 degrees C. or 37 degrees C.

EDTA: Ethylene Diamine Tetraacetic Acid (17%): Lubricant, remove inorganic

Chelators may detach biofilms adhering to root canal walls. This may explain why an EDTA irrigant proved to be highly superior to saline in reducing intracanal microbs despite the fact that its antiseptic capacity is relatively limited (Cohen path ways). **EDTA works by replacing Ca ions with Na and make the dentin softer.**

"EDTA retained its calcium-complexing ability when mixed with NaOCl, but EDTA caused NaOCl to lose its tissue-dissolving capacity, with virtually no free chlorine detected in the combinations. Clinically, this suggests that EDTA and NaOCl should be used separately."

Nygaard-Ostby 1957 introduced EDTA.

RC Prep Contains 3.8% **EDTA**, Urea peroxide and propylene glycol which was introduced by Stewart and doesn't contain Carbowax unlike the previous ones.

Schilder: EDTA is self limiting after 7hrs

Calt & Serper 2002 JOE: Time dependent activity of EDTA. **10 ml of 17% EDTA 1 min** enough for smear layer removal and 10 minutes can cause too much dentinal erosion

Owing to its cationic nature, CHX is capable of electrostatically binding to the negatively charged surfaces of bacteria damaging the outer layers of the cell wall and rendering it permeable

CHX has Substantively effect, It is antimicrobial and does not remove smear layer

White and also Mulover (M&M) talked about substantively by binding to dentin (for 72 h). **Emilson CG, Ericson**: Uptake of chlorhexidine to hydroxyapatite. it seems that residual antimicrobial activity of CHX in the root canal system remains for up to **12 weeks.**

Jeansonne MJ, White RR. A comparison of 2.0% chlorhexidine gluconate and 5.25% sodium hypochlorite as antimicrobial endodontic irrigants. J Endod 1994: No difference in antimicrobial activity

between 2% chlorhexidine and 5.25% NaOCl, but NaOCl has added advantage of tissue dissolution. **Chlorhexidine is an excellent irrigating alternative for NaOCl allergic patients, perforations, and teeth with open apices.**

Böttcher (JOE-2015): The results of their study indicate that 2% CHX solution was detected for 48 hours and 7 days with a low percentage of viable cells.

Raheja J (2015, RCT, JOE): Evaluation of efficacy of chlorhexidine intracanal medicament on the periodontal healing of concomitant endodontic-periodontal lesions without communication: an interventional study. **CHX may be used as an effective intracanal medicament for promoting periodontal healing in concomitant endodontic-periodontal lesions.**

Basrani: The **substantively depends on the concentration** not on the mood of application either as gel or liquid. Overall, because of its substantivity, CHX as an intracanal medicament/irrigant may delay the coronal recontamination of the root canal system.

Siqueira JF, Jr., De Uzeda M: Evaluation of the antibacterial activities of calcium hydroxide, chlorhexidine, and camphorated paramonochlorophenol as intracanal medicament= no significant difference

Safavi and Spangberg talked about antimicrobial effect of CHX. **2% CHX** kill E. Feacalis (gr+, facultative, diplococcic) in retreatment cases.

Siqueira, Lima, Evans: Susceptibilities of Enterococcus faecalis biofilms to some antimicrobial medications. J Endod, 2001: Notably, 2% CHX was very effective in eliminating a biofilm of E. faecalis, Also reported that it reduced the bacteria as effective as CaOH.

Basrani: CHX mixed with NaOH gives a **brown precipitate (that contains para-chloroaniline**). However, based on ***in vitro*** **study by Thomas (JOE, 2010**), the reaction mixture of NaOCl and CHX does not produce PCA at any measurable quantity, and further investigation is needed to determine the chemical composition of the brown precipitate. **Ekim Onur Orhan (JOE, 2016)** proved that the participates do not contain PCA.

Delgado (JOE, 2010) showed that chlorhexidine gel had a significantly higher antimicrobial efficacy as measured by the number of CFUs and the percentage of viable cells than Ca(OH)2 against E.faecalis.

Siqueira (2011, JOE) found that treatment protocols using irrigation with either NaOCl or CHX succeeded in significantly reducing the the number of bacterial taxa and their levels in infected root canals, with no significant difference between these substances. However, each of the irrigation protocol is effective against different taxa.

Calcium hydroxide ($Ca[OH]_2$) is used widely as an intracanal medicament in root canal treatment to reduce residual bacteria (Messer). It has been used in endodontics in various clinical situations. It inhibits osteoclastic activity (Safavi), degrades bacterial lipopolysaccharides (Safavi), dissolves soft tissues (Hasselgren), and promotes apexification. Even though the use of $Ca(OH)_2$ has now subsided with the use of mineral trioxide aggregate and similar biomaterials, such as bioceramics, it is a traditional pulp capping material used in vital pulp treatments

Herman 1920: introduced CaOH as an intracanal medicament in necrotic teeth

Heithersay 1975: CaOH kills most bacteria due to its pH of around 12.5

Sjogren and Sundqvist: minimum use of CaOH for 7-10 days.

Siqueira talked about antimicrobial mechanism of CaOH:
·Hydroxyl ions create free radicals destroying components of bacteria cell membranes.
·Free radicals (hydroxyl ions) react with bacterial DNA inhibiting DNA replication and cell activity.
·Increased pH (12.5) alters enzyme activity disrupting cellular metabolism and structural proteins.
·Ca(OH)2 effective when in direct contact with bacteria which may not always be possible such as bacteria located in dentinal tubules or in the center of bacterial colonies. pH in tubules is increased, but only up to 8-11 and this is a mechanism can stop resorption (Tronstad).
·Certain bacteria such as enterococci tolerate high pH levels of 9-11.
·Vehicle used to deliver Ca(OH)2 must not alter the pH significantly.

Orstavik: NaOCl canal irrigation reduced the bacteria level by only 61.9%, but use of Ca(OH)2 in the canals for 1 week resulted in a **92.5% reduction**. These researchers concluded that Ca(OH)2 should be used in infected cases to more predictably obtain disinfection. Superior antimicrobial effect of CaOH when used long term. However, **Sathorn (IEJ)** found that Calcium hydroxide has limited effectiveness in eliminating bacteria from human root canal when assessed by culture techniques

Gomes: 2% CHX gel + Ca(OH)2 showed better antimicrobial activity than Ca(OH)2 manipulated with sterile water.

Turkun: **Calcium hydroxide was an effective solvent for necrotic tissue as a paste** but not as a solution. Pretreatment of necrotic tissue with Ca(OH)2 increased its solubility in 0.5% NaOCl. While 5% NaOCl plus ultrasonic irrigation produced cleaner root-canal walls at the middle and apical thirds, 0.5% NaOCl used with the same technique achieved no root-canal cleaning. However, pretreatment of root canals with Ca(OH)2 paste increased the effectiveness of 0.5% NaOCl plus ultrasonic irrigation, except in the coronal third of the root canal. CaOH shows tissue dissolution but slower than bleach and also bleach works better after we put CaOH in the canal. Also **Hasselgren G, J Endod 1988** confirmed these findings.

Madison compared the intracanl placement of CaOH: Lentulo>injection (Calasept)>K file.

Waltimo, Orstavik, Siren, Haapasalo 1999: In vitro study, showed that combining calcium hydroxide with sodium hypochloride or CHX may provide a wide-spectrum antimicrobial preparation with a long-lasting effect. **More efficient than CaOH alone.**

McCormick (1983) Osteoclastic cells (osteoclasts & PMNs) prefer acidity. The high pH of Ca(OH)2 antagonizes their action.

Hargreaves et al, 2008 JOE
✓ Ca(OH)2 denatures IL-1, TNF and CGRP by 50%-100%.
✓ Denaturation of these pro-inflammatory mediators is a potential mechanism by which Ca(OH)2 contributes to the resolution of periradicular periodontitis.

Tronstad: Ca(OH)2 effective when in **direct contact with bacteria** which may not always be possible such as bacteria located in dentinal tubules or in the center of bacterial colonies (Same finding was shown by **Bystrom**) pH in tubules is increased, but only up to **8-11**. He mentioned that CaOH might be effective in resorptive case by inhibiting osteoclastic activity.

Andreasen: Recommended use of CaOH < 1m. **Long term use of CaOH increase risk of root fracture (in sheep). Trope** rec 6 months use for internal resorptions. **Tamse**: 2 weeks

Z. MohammadI: CaOH has a wide range of antimicrobial activity against common endodontic pathogens but is less effective against Enterococcus faecalis and Candida albicans. Calcium hydroxide is also an effective anti-endotoxin agent. However, its effect on microbial biofilms is controversial.

Safavi and Nichols: CaOH inactivates LPS. CaOH is ineffective against E. Faecalis.

Yared&Bou Dagher: To evaluate the influence of apical enlargement on bacterial infection during treatment of apical periodontitis. There is **no difference** in the antimicrobial effect of CaOH after 1 week placement in canals enlarged to file 25 or file 40

CaOH dissolve tissue (**Turkan, Hasselgrain**); anti-inflammatory (**Hargreaves**); anti-resorptive by alkaline environment (**McCormick**); osteoinductive potential of bone (**Kawakami, Nakamura: cause differentiation of mesanchimal cells of PDL to osteoblasts and cementoblast**); antibacterial.

E. Faecalis is resistant to Calcium Hydroxide due to **proton pumping**. Resistant up to pH 11.5. Above that it kills it. **Evans:** E. Faecalis proton pump resists high pH of calcium hydroxide.

E. faecalis expresses various virulence factors including **lipoteichoic acid** (LTA), peptidoglycan, aggregation substance, surface adhesins, sex pheromones, lytic enzymes such as gelatinase and hyaluronidase, and cytolysin. Of these virulence factors, LTA is considered one of the most important etiologic factors that is responsible for inflammatory responses and tissue damages. Although it has been suggested that the presence of proton pump make E.faecalis resistant to CaOH, in **2011 (JOE) Jung Eun Baik showed that calcium hydroxide attenuates the inflammatory activity of E. faecalis LTA through deacylation of the LTA.**

Lambrianidis: The removal of Ca(OH)2 is frequently incomplete, resulting in a residue covering 20% to 45% of the canal wall surfaces, even after copious irrigation with saline, NaOCl, or EDTA. Residual Ca(OH)2 can shorten the setting time of zinc oxide eugenol–based endodontic sealers. Most notably, it may interfere with the seal of the root filling and compromise the quality of treatment. This finding is in agreement with **KIM study Influence of calcium hydroxide intracanal medication on apical seal. Int Endod J 2002.** The Ca(OH)2 groups showed significantly more dye leakage than the non-medicated control group. However, **Bumgartner** said that CaOH can be effectively removed using NaOCL or EDTA. Kim questioned study of Kontakiotis who said CaOH2 dressing does not effect the seal of the permanent root canal filling. Questions whether methylene blue is useful for CaOH2 studies. CaOH2 decolorizes methylene blue. This study used the fluid transport method for measuring leakage.

Baumgartner: Smear layer contains of two layers: a thin layer on the surface of the canal wall 1-2 microns thick and a layer in the dental tubules up to 40 microns. Frequency and depth was unpredictable and the smeared material appeared friable and only loosely adherent to the dentinal tubules.

Turkun: Smear layer is made up of inorganic and organic (pulp, bacteria, bacterial by-products) debris.

McComb & Smith: First to describe the smear layer under the SEM Vol1 JOE (1975-first year). Used NaOCl & REDTA

Foster (1993) Removal of smear layers facilitates diffusion of Ca(OH)2 to kill bacteria (Bystrom: OH moiety is bactericidal). However, **Haapasalo (JDR, 1987)** suggested that smear layer removal can facilitate bacterial invasion into dentinal tubules. In this case, **Oguntebi** suggested that these bacteria can act as reservoir and cause re infection.

Yang J Endodon 2002: Given that the smear layer produced during root canal preparation promoted adhesion and colonization of P. nigrescens to the dentin matrix, it might also increase the likelihood of canal reinfection.

Yamada (1983 JOE): The most effective way to remove organic and inorganic components of smear layer is **10 ml 17% EDTA and then 10ml 5.25% NaOCl**.

Moon (JOE, 2010): In curved canal, final rinse with NaOCl after the use of EDTA had no additional effect on sealer penetration. Complete debridement with a 1-minute application of EDTA remains a challenge in the apical area of curved canals.

Shahravan Arash 2007 (JOE): Smear layer removal improves the **fluid-tight seal** of the root canal system whereas other factors such as the obturation technique or the sealer, did not produce significant effects.

Baumgartner 1987, Goldman reported that EDTA alone can not remove smear layer and it needs NaOCL to remove the organic part.

Haapasalo M 2012 (JOE): Within dentin canals, bacteria in established biofilms are less easily killed by endodontic medicaments than bacteria in young biofilms.

Taylor & Jeansonne (1997): Coronal leakage cumulatively **reduced** by removal of smear layer, use of AH26 and vertical compaction. **Madison also Evans and Simon** reported that removal has no effect on apical seal. However, **Cergneux (IEJ)** studied apical seal following EDTA or ultrasonic/NaOCl used. Found that a better seal occurred when smear layer was removed with EDTA. **Smear layer removal improves the apical seal.**

White, Goldman (1984): smear layer removal improves the sealer penetration into dentinal tubules. Least sealer penetration occurs in the apical third. Also **Astrit Kuçi (2014, JOE)** confirmed these findings. They stated that greater sealer penetration could be achieved with either the MTA Fillapex–cold lateral compaction combination or with the AH26–warm vertical compaction combination. Smear layer removal was critical for the penetration of MTA Fillapex; however, the same did not hold for AH26.

One of the questions regarding the irrigation protocol is that can age and sclerotic dentin affect the efficacy of irrigation and time required for smear layer removal!? Ozdemir (2012, JOE) concluded that treatment with EDTA + NaOCl for 1 minute appeared to be the best experimental combination in both young and old dentins for different reasons. In young dentin, extending the treatment time of EDTA + NaOCl over 1 minute does not significantly alter the chemical and ultramorphologic structure and thus appears to be unnecessary. In old dentin, extending the treatment time of EDTA + NaOCl over 1 minute leads to excessive demineralization and erosion and thus should be avoided.

QMIX is made of Polyaminocarboxylic Acid (chelating agent), Bisguanide (anti-microbial), a surfactant and deionized water. QMIX contains EDTA, CHX. Studies have shown 99.99% bacterial reduction rate but it doesn't have tissue dissolution. QMIX is a final rinse and is capable of disinfecting and removing smear layer

Eliot C, Hatton JF: All irrigants removed smear layer more effectively at the coronal and middle levels compared to the apical level ($p < 0.001$). Analysis showed all three **QMix formulations were superior to**

EDTA in smear layer removal and exposure of dentinal tubules in the root canal system in single-rooted teeth.

Torabinejad: MTAD: Doxycycline, Acetic Acid and Detergent (Tween80) = Remove the smear layer and inhibit the E. faecalis

Hoshino: developed Triple Antibiotic Paste from **Ciprofloxacin, Metronidazole and Minocycline**. In the double paste there is no Minocycline.

Molander (Sweden, IEJ): Microbiological evaluation of clindamycin as a root canal dressing in teeth with apical periodontitis. **Clindamycin offered no advantage over conventional root canal dressings, such as calcium hydroxide, and it is therefore not recommended for use in routine endodontic therapy.**

Richman: First described ultrasonic in endodontics.

Ahmad, Pitt Ford: Ultrasonic works by acoustic streaming & not cavitation.

Cunningham reported removing smear layer using ultrasonic activation.

Walker: 3 min passive activation of sonic or ultrasonic produced significantly cleaner canals than files alone BUT there is NSD between sonic and ultrasonic.

Huque & Iwaku 1998 IEJ: Ultrasonic with 5.5% NaOCl is effective in eradicating bacteria and removing smear layer from infected dentin (artificial smear layer infected with Actinomyces, Fusobacterium, Streptococcus).

Caron G: Cleaning efficiency of the apical millimeters of curved canals using three different modalities of irrigation activation: an SEM Study, 2006. The **EndoActivator** was shown, again, to produce statistically significantly cleaner canals as compared to the controls and RinsEndo. Study emphasis was on the apical one-third.

Surendar Ramamoorthi (2015-AEJ): activation of irrigants using EndoActivator can be considered an effective method for reducing postoperative pain!!!!

Kamran Safavi (2012, JOE) compared the antibacterial effect of nonactivated single-irrigation protocol (NAI) that used only 1% NaOCl with a passive ultrasonic multi-irrigation protocol (PUI) that used 1% NaOCl, 17% ethylenediaminetetraacetic acid, and 2% chlorhexidine. Also, the effect of a second-visit instrumentation after intra-appointment calcium hydroxide (CaOH2) was evaluated in bacterial elimination. **NAI and PUI rendered canals 80% and 84% bacteria free, respectively, at the end of the first visit.** After CaOH2 medication the total sample (NAI + PUI) had increased to 87% bacteria free, and the second-visit instrumentation resulted in a total of 91% bacteria free. **These differences were not significant (P > .05).**

Liang (2013, JOE) performed randomized clinical trial investigating the effect of ultrasonic activation of irrigant on radiographic healing after RCT. It was found that **root canal treatments with and without additional ultrasonic activation of the irrigant contributed equally to periapical healing.**

Markus Haapasalo (JOE,2010): The **Synergistic** Antimicrobial Effect by Mechanical Agitation and Two Chlorhexidine Preparations on Biofilm Bacteria: The **combined use of mechanical agitation and chlorhexidine** had a more pronounced antimicrobial effect against the biofilms than either one alone.

Instrumentation

Aminoshariae (IEJ, 2015): The best current available clinical evidence suggests that contemporary chemomechanical debridement techniques with canal enlargement techniques do not eliminate bacteria during root canal treatment at any size.

Schilder: Cleaning and shaping the root canals (1974) Journal: Dental Clinic North America

Root canal preparation has been described as instrumentation, biomechanical instrumentation and chemomechanical instrumentation. Intracanal medications are still important in endodontics, but only in canals whose walls have been scrubbed smooth of retained tissue prior to their use. Even if residual necrotic tissue in root canals is uninfected, tissue degradation products leaking through main or accessory foramina create lesions in the adjacent attachment apparatus if total obturation is not achieved.

Mechanical objectives

1) Root canal preparation should develop a continuously tapering shaping (CTS) from the root apex to the coronal access cavity

2) The cross sectional diameter of the preparation should be narrower at every point apically and wider cervically

3) Root canal preparation should flow with the shape of the original canal

4) The apical foramen should remain in its original spatial relationship both to the bone and to the root surface. 5) The apical opening should be kept as small as practical in all cases.

6) Outline of the funnel in the apical portion of the root canal should be round in all cases, but in the middle and cervical third it may or may not be desirable

7) Cross sectional diameter has to be narrower at every point apically and wider at every point coronally

8) The sole exception to this principle is incases of internal resoprtion where absolute adherence to this rule would grossly weaken the remaining tooth structure

9) Foramen transposition most commonly takes 2 forms – development of an elliptical or teardrop foramen, and outright root perforation

10) Apical foramina are usually found slightly short and to the side of the radiographic apex.

11) Tapering funnel preparation from the root apex to the coronal access cavity

12) Greatest problem lies in the apical portion of the canal, and the greatest care must be taken to maintain the direction of the canal curvature.

There are 2 cautions –

1. No straightening is permitted in the apical few millimeters
2. Unconscious straightening is dangerous

· Position of the foramen remain in its original shape, formanen transportation, tear drop foramen

Biologic objectives of cleaning and shaping:

· Confine instrumentation to the root canals

· Beware of forcing necrotic material beyond the foramen during canal preparation

· Remove all tissue debris from the root canal system

· Try to complete the cleaning and shaping of single canaled teeth in one visit and, whenever possible, prepare multi-canaled teeth one at a time

· Create sufficient space during canal enlargement to receive intrcanal medicaments and to accommodate small amounts of periapical exudates

Clinical Principles common to all canal preparation

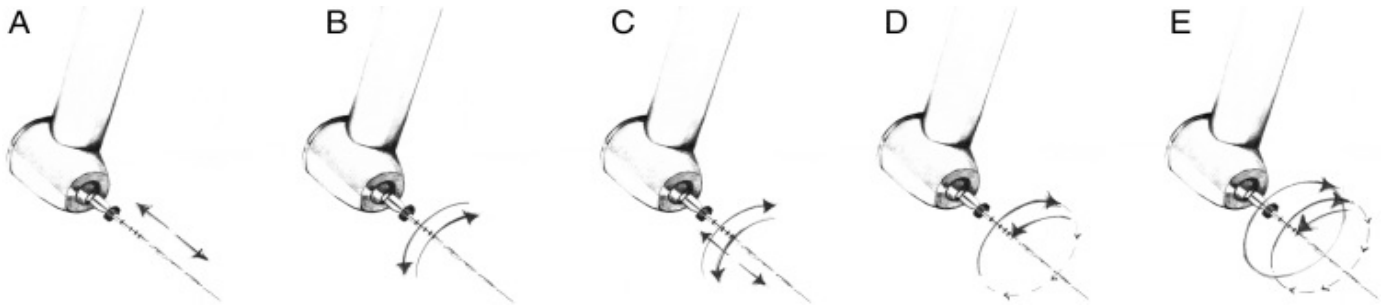
1. Irrigation is abundant
2. Never skip instruments

3. Never skip to the next instrument until the previous one fits loosely in the canal
4. When the next file doesn't fit to the apex, consider using a cut off file of the previous of the previous file size as an intermediate instrument
5. In general, the narrower and more curved the canal, the more it must be shaped with files rather than reamers
6. Reamers and files that shows sign of irregularities should be discarded immediately
7. Loss of canal patency, blocked canal is regained by irrigation, use of precurved file
8. Partially calcified canal can be negotiated successfully

Review of techniques:

Roane, Sabala: Balanced Force
Torabinejad; Kelly, Weine ; Walton: Passive Step back
Marshall – Crown Down Pressure less = You extrude less debris from apex compared to step back; **Silva (JOE, 2014)** stated that all systems caused apical debris extrusion. However, reciprocating systems like WaveOne were associated with less debris extrusion when compared with a conventional rotary retreatment system.

Nicola Maria Grande, Stephen Cohen (JOE 2015): Current Assessment of Reciprocation in Endodontic Preparation: A Comprehensive Review: Reciprocation movement (RM) is defined as a repeated backward and forward (CW/CCW) movement; this reciprocal movement can be applied to many endodontic files, and it has been extensively used in endodontics for many years. There are many variations of RM, including complete reciprocation (**oscillation**), partial reciprocation (**rotational effect**), and hybrid reciprocation (**combined movements**). Hybrid reciprocation can be fixed or flexible (ie, they can shift from one type of reciprocation to the other in the canal based on mechanical resistance and torque).



Different types of RM for endodontic instrumentation: (A) complete reciprocation with vertical oscillations (Racer and Self-Adjusting File), (B) complete reciprocation with horizontal rotational oscillations (Giromatic, Intra-Endo 3 LD, Dynatrak system, M4 Safety Handpiece, Endo-Gripper, NSK TEP-E10 R, Endo-Eze AET system, Tilos system, and Endo-Express SafeSider), (C) complete reciprocation with combined oscillations (Canal Finder System, Excalibur, Canal-Leader 2000, Endolift, Endoplaner, and EndoPulse system), (D) partial reciprocation with rotational effect (ATR Teknica, WaveOne, WaveOne Gold, and Reciproc), and (E) hybrid reciprocation (TF Adaptive/Elements motor).

Crown-down (**Ruiz-Hubbard & Gutmann** 1987 JOE) and balanced-force (**McKendry 1990 JOE**) extruded less debris than step-back filing.

Sepic AO, Pantera EA, Jr., Neaverth EJ, Anderson RW. A comparison of Flex-R files and K-type files for enlargement of severely curved molar root canals. Journal of Endodontics 1989.

Less apical transportation with the balanced force technique when compared with a step-back technique in canals exhibiting both more and less than 45 degrees of curvature.

Teixeira JM (2015): WL and the apical preparation size did not have a significant effect on bacterial extrusion when performing **reciprocating** instrumentation.

Martinho, Gomes (JOE, 2014) suggested that both single-file reciprocating systems (ie, **WaveOne** and Reciproc instruments) and rotary systems (ie, **ProTaper** and Mtwo instruments) showed **similar effectiveness in reducing endotoxins and cultivable bacteria** from primarily infected root canals, but they were not able to eliminate them from all root canals analyzed. This finding was also confirmed in a cultural independent method QPCR by **Siqueira (JOE,2016**). It was also confirmed by **Daniel Kherlakian (2016, JOE)** that reciprocating systems and the continuous rotary system were found to be equivalent in regard to the incidence of postoperative pain and intake of analgesic medication at the time points assessed.

Pineda and kuttler: Exit of root canal can be anywhere up to 3mm short distance from the radiographic apex
Kuttler 1955: Size of apical constriction 0.5mm in young and 0.65mm in adults (distance btw apical constriction and foramen). Also the size of apical foramen diameter of the foramen is 502 μm in individuals 18 to 25 years of age and 681 μm in those over age 55, which demonstrates the growth of the AF with age.

Green: 50% of canals are deviated from the radiographic apex. Also Levy & Glatt talked about canal deviation.

E lAyouti: A radio graphically determined WL 0-2mm short of the radiographic apex causes unintentional over instrumentation in 50% of PM and 22& of molars.

Palmer, Weine: 50% of the teeth instrumented **to radiographic apex they are actually 1 mm out of apex.**

Iqbal 2010; Baumgartner: Over instrumentation can be minimized by completing coronal flaring before WL determination due to change in the WL.

Weine 1975, or Caldwell 1976, or Khurana 2011: Working length in curved canals can be shorter after instrumentation due to straightening of the canals and eventually can cause over-instrumentation

Ibarrola (1999 JOE): Preflaring canals permits WL files to reach apical foramen more consistently with Root ZX.

Stabholz: Better tactile sense at the apical constriction after preflaring.

Shovelton: Preflaring remove more microorganism and reduce the bacterial load in vital cases because they are more in the coronal part in vital cases.

Álvaro Henrique Borges (JOE, 2016) showed that for all file systems, cervical preflaring reduced the amount of apically extruded debris when compared with no cervical preflaring ($P < .05$).

Wein: The apical root canal often is tapered, or walls are parallel to each other, or the canal has multiple constrictions. Some authors therefore have recommended the following **termination points: 1 mm from the apex when no bone or root resorption has occurred; 1.5 mm from the apex when only bone resorption has occurred; and 2 mm from the apex when both bone and root resorption have occurred.**

Sjogren, Hugland: For **vital** cases, clinical and biologic evidence indicates that a favorable point at which to terminate therapy is **2 to 3 mm short of the radiographic apex**. This leaves an apical pulp stump, which prevents extrusion of irritating filling materials into the periradicular tissues. With **pulp necrosis**, bacteria and

their by-products may be present in the apical root canal, which could jeopardize healing. Studies have shown that, in these cases, a **better success rate is achieved when therapy ends at or within 2 mm of the radiographic apex.**

Langland: Most favorable prognosis was obtained when procedures were terminated at the AC, and the worst prognosis was produced by treatment that extended beyond the AC. Procedures terminated more than 2 mm from the AC had the second worst prognosis.

Davis & Joseph 1971: Teeth that were fully instrumented, but filled short of the radiographic apex had best healing. **Seltzer & Bender 1963 &67**: human and monkey study with healing evaluation at 3 months; **overfill = persistent inflammation. Serene reported this inflammation is due to c3 complement activation.**

Walton, 2005 JOE (Meta-Analysis of literature): Obturating materials extruding beyond the radiographic apex correlated with a decreased prognosis.

Bergenholtz: There was a significant higher incidence of periapical lesions on overfilled roots than on roots without excess filling.

Topçuoğlu: performing coronal flaring prior to canal preparation reduced the amount of apically extruded debris.

Endodontic files classic review:

Webber, Moser, Heuer: Triangular instruments more efficient initially but lost sharpness quickly. Square had greater retention of sharpness.

Pliet & Sorm 1973: Triangular instruments cut more efficiently than square files

Lester B. Chernick: Torsional tests and scanning electron microscope examination revealed that endodontic files twisted in a counterclockwise manner were extremely brittle in comparison to those twisted in a clockwise manner. This study is opposite to Roan study which shows separation is more likely in clockwise rotation.

Miserendino (1985, JOE): Significantly greater cutting efficiency occurred with the newly designed S file and traditional Hedstrom files over other types of hand instruments. The tip geometry of the file has the greatest impact on the cutting efficacy of the file COMPARE TO FLUTE DESIGN.

Kazemi 1995 JOE: It was shown that all files evaluated rapidly deteriorated when machining dentin. This decline in efficiency was significant but different within, as well as, among brands. It was suggested that endodontic files be disposable.

Seto: Machined files exhibit less ductility than twisted files prior to fracture and may be more susceptible to torsional failure clinically.

Tepel and Schafer: Compared different manual hand instruments. Best instrument results were obtained by flexible instrument with noncutting tip. Also they found that SS K-file have better cutting efficacy than NiTi.

Yucel and Henry: Never cut the canals dry. Lubricant increases efficiency by 200%. Water and 2.5% sodium hypochlorite solutions have equivalent lubricant effects. The most common breakage of file happens with headstrom. **Plastic deformation is the main cause of loss of cutting efficiency.**

Walia, Brantley & Gerstein: 1st description of Nitinol (2-3 times more flexible than SS files) developed in Naval Ordinance Lab (1988).

Haikel: Talked about properties of NiTi: **NiTi has 2 phases: austenite (A crystalline unstressed phase of stainless steel and nickel titanium alloy) and martensitic (In nickel titanium alloy, this more flexible form occurs as the result of thermal changes or the application of stress)**. The ability to cycle between these 2 states is due to NiTi having the property of super elasticity and shape memory. Phase transition occurs with rapid stress on the file, therefore use at a constant speed. Files are weakest during phase transition and may fracture at this time (cyclic fatigue). Radius of curvature was found to be the most significant factor in determining the fatigue resistance of files. Cyclic fatigue as a major cause of failure.

Transporting: 3 studies of 1) **Esposito** 2) **Schafer&Tepel** 3) **Kuhn**: talked that there is a less chance of transportation using NiTi and they maintain the original shape of the canal compared to SS K files.

Pettiette & Trope 1999: Less deviation of canal with NiTi files vs SS. Less procedural errors with NiTi files vs SS. Maintaining the original canal shape after instrumentation leads to a better prognosis of endodontic treatment.

Yoldas: compared the effect of hand files and rotary files on dentin after canal preparation. They concluded that rotary instruments caused more dentinal defects, such as craze lines and cracks, which possibly could develop into fractures after restorative treatment.

Does rotary instrumentation remove more bacteria?
Orstavik:
1) There was no detectable difference in colony-forming unit count after NiTi rotary or stainless-steel hand instrumentation.
2) NiTi rotaries are not more effective for microbe elimination than hand instrumentation. Profile and 1.25% NaOCl decreased bacteria 62%, 1 week CaOH2 decreased bacteria 93%.

Walton: talked about **apical clearing**. **Tapering preparation permits** 1) better debridement of apical preparation 2) reduces over-instrumentation of the foramen and 3) improves ability to obturate.

Apical clearing: A technique that involves enlargement of the apical preparation followed by dry reaming to remove dentin debris and to produce a more defined apical stop

Gonzalez Sanchez 2010: Small patency files extended 1mm beyond the apical foramen found no transportation. **Goldberg and Massone 2002** found that using big files in patency cause apical transportation (61% #25, 25% #10).

Jorge Vera and ana arias (JOE, 2012) reported that maintaining apical patency improves the delivery of irrigants into the apical third of large human root canals.

Peters OA: You can minimize the fracture rate of Protaper files when a patent canal (glidepath) is present.

Does sterilization affect NiTi?

Cunningham: Neither the number of sterilization cycles nor the type of autoclave sterilization affects the torsional properties, hardness, and microstructure of stainless steel and NiTi files.

Pruett, Clement, Carnes (1997):
Cyclic fatigue testing of nickel-titanium endodontic instruments. NiTi instruments fracture within their elastic limit and without any signs of previous permanent distortion. Rotation subjects NiTi to both tensile and compressive forces in the area of the canal curvature; this produces a very destructive form of loading.

Cyclic fatigue: Instrument failure due to repetitive stress.

35% of canals are left untouched by instrument: **OVE A peters (IEJ 2001)** also **Metzger (JOE-2010)** showed that protaper rotary files leave **44.6%** of the canals untouched.

Torabinejad: concluded that "because of long oval canals, larger canal tapers in the buccal–lingual direction, wider ranges in the apical diameters of canals, and the lack of technology to measure these diameters, **it is very difficult if not impossible to adequately debride all canals by instrumentation alone.** Therefore, **Orstavik and Trope** determined that enlarging canals to greater than the traditionally recommended apical sizes was the only way to remove cultivable bacteria from the canal effectively. Also **Bumgartner and Marshal** suggested that the larger apical sizes optimized irrigation and disinfection and facilitated mechanical elimination of microbes. A similar study concluded that an increase in the size of canal instrumentation at working length produced an increase in canal cleanliness. Irrigant volume, the number of instrument changes, and the depth of penetration of irrigant needles were less important factors contributing to canal debridement.

Master apical file size – smaller or larger: a systematic review of healing outcomes: A. Aminoshariae (IEJ, 2015): Due to the variety of methodologies and different techniques used to measure outcome for master apical file enlargement, it was not possible to standardize the research data and to apply a meta-analysis. Seven articles were identified that met the inclusion criteria. Five of the seven articles generally concluded that canal enlargement reduced bioburden in the root canal system. Two articles reported no difference in canals enlarged to size 25 or 40. The results of the systematic review confirmed that more evidence-based research in this area is needed. For patients with necrotic pulps and periapical lesions, enlargement of the apical size would result in an increased healing outcome in terms of clinical and radiographic evaluations.

Carol Anne (Michigan) minimally invasive dentistry: preservation of a healthy set of natural teeth for each patient should be the objective of every dentist. The application of a systematic respect for the original tissue while maintaining the natural dentition= Dentin preservation. **Minimally invasive (MI)= Magnification and illumination.**

Peters OA: As the TRU Shape rotating it makes an **actual envelope of motion** that is larger than nominal file size. The S curve in true shapes help this envelope of motion greater than the actual nominal size of file. This system follows the hooks law of spring. It was shown that there is up to **36% better dentin preservation** with TRU shape compared to standard file with the same tip and taper (20/06) and **less apical transportation.**

Sedgley: Vital dentin 3.5% harder; biomechanical properties are not significantly altered after root canal treatment and teeth do not become more brittle after RCT. **This is cumulative loss of tooth structure that weaken the tooth.**

Reeh: Reduction in tooth stiffness as a result of endodontic and restorative procedures? Endodontic procedures have only a small effect on the tooth, reducing the relative stiffness by 5%. This was less than that of an occlusal cavity preparation (20%). The largest losses in stiffness were related to the loss of marginal ridge integrity. **MOD cavity preparation resulted in an average of a 63% loss in relative cuspal stiffness.**

K. Zelic (IEJ, 2015): Mechanical weakening of devitalized teeth: three-dimensional Finite Element Analysis and prediction of tooth fracture: Teeth with two-surface composite restorations that underwent root canal treatment are less resistant to high occlusal load, but the main contribution to their weakening arises from access cavity preparation. Canal enlargement does not contribute to this process substantially.

Iatrogenic events:

Ahmad A. Madarati (JOE, 2013) performed a **systematic review** on management of intracanal separated instruments. Factors Influencing Removal of Separated Instruments are:

1) **Tooth Factors:** In maxillary teeth, in anterior teeth, When the fragment extends into the coronal third of the root canal, When the fragment is located before the root canal curvature, When the instrument separates in straight or slightly curved root canals.
2) **Separated instruments factors**: It is generally believed that NiTi rotary instruments are more difficult to remove compared with SS ones: They tend to thread into root canal walls because of their rotary movement, They have greater tendencies to fracture repeatedly during removal procedures, particularly when ultrasonics is used Clinical observation has revealed that fragments of NiTi instruments in curved root canals tend to lie against the outer root canal wall and do not remain in the center of the canal because of their flexibility. They usually fracture in short lengths, especially after torsional failure; the longer the fragment, the higher the success rate of retrieval because longer fragments are usually more coronally located.

Ruddle's technique for removing the broken instrument (From from Madarati JOE): "A staging platform is prepared around the most coronal aspect of the fragment by using modified Gates Glidden burs (no. 2–4) or ultrasonic tips. The Gates Glidden bur is modified by grinding the bur perpendicular to its long axis at its maximum cross-sectional diameter. The platform is kept centered to allow better visualization of the fragment and the surrounding dentin root-canal walls; therefore, equal amounts of dentin around the fragment are preserved, minimizing the risk of root perforation. The ultrasonic tip is activated at lower power settings, so it trephines dentin in a counterclockwise motion around a fragment with right-hand threads and vice versa. With this trephining action and the vibration being transmitted to the fragment, the latter often begins to loosen and then "jumps" out of the root canal. Other root canal orifices in the tooth, when present, should be blocked with cotton pellets to prevent the entry of the loose fragment. If little care is taken and excessive pressure on the ultrasonic tip is applied, the vibration may push the fragment apically or the ultrasonic tip may fracture, leading to a more complicated scenario. Also, to prevent separation of the ultrasonic tip, it is important to avoid unnecessary stress by only activating it when in contact with root tissue"

Nevares (JOE, 2010) assessed the success rate of Ruddle technique for removing broken instruments which has proposed a technique for the removal of metallic instrument fragments from the root canal by using a combination of Gates-Glidden burs, microscopic magnification, and ultrasonic tips. The overall success rate (removal and bypassing) was 70.5%. **In the visible fragment group, the success rate was 85.3% and in the nonvisible fragment group it was 47.7%.** Success rates were significantly higher when the fragment was visible.

Crump & Natkin (1970): A separated file in a canal does not mean failure. It depends upon the **location** of the file and the **prior debridement/Shaping** of the canal system.

Spilli et al (systematic review): 3.3% happen. In the hands of skilled endodontists prognosis was not significantly affected by the presence of a retained fractured instrument. Mentioned the factors that affect the prognosis of broken instrument **1) Location 2) Time 3) Diagnosis**

Panitvisai, Sathorn and Messer (JOE, 2010): Mean healing for teeth with a retained instrument fragment was 91%. **Overall, 80.7% of lesions healed when a periapical lesion was present, compared with 92.4% remaining healthy when no lesion was present initially** ($P < .02$). On the basis of the current best available evidence, **the prognosis for endodontic treatment when a fractured instrument fragment is left within a root canal is not significantly** reduced. However, this finding might not be accurate for teeth with periradicular lesions (Spilli)

Grossman (OOO, 1969) concluded that separated instruments affected the outcome only when a periapical lesion was present.

Strinberg et al: 19 % higher incidence of failure following broken instrument

Krell (1984) & Ngai (1986): rec use of ultrasonic files to enlarge canal space around post/Ag points/separated instrument. Johnson recommended **16 min ultrasonic activation** for removal of Parapost.

Nagai et al: reported a success rate of 73% with ultrasonic removal of broken instruments in 99 extracted teeth. In vivo, they successfully retrieved the objects from 26 of 39 teeth (66.6%), while in 6 other teeth (15.4%), the objects were successfully bypassed without being retrieved. The time required retrieving the objects varied from 3 to 40 min.

Stephe Davis (JOE, 2010) showed that injurious heat transfer occurs in less than 1 minute during dry ultrasonic instrumentation of metallic posts. Cycles of short instrumentation times with active coolants were effective in reducing the probability of tissue damage when teeth were instrumented dry. With as little as 20 seconds of continuous dry ultrasonic instrumentation, the consequences of thermal buildup to an individual tooth might contribute to an injurious clinical outcome

Please notice spite successful use of ultrasonic in file removal, the attempt might lead to ledge formation, over enlargement, and transportation of the prepared root canal. Excessive enlargement and formation of irregularities in canal shape can predispose teeth to vertical root fracture. Furthermore, ledge formation, a possible stress concentration point, is one of the underlying causes of root fracture (Souter, Messer JOE 2005)

Bahcall JK: Dentist can best prevent this occurrence by using hand files before rotary files, creating a straight-line (**glide path**) access into a canal, and **preflaring** the coronal portion before using rotary files in the apical third of the canal. **Torabinejad**: Preflaring of the canal was far less likely to result in file separation.

The best prognosis is when the instrument is broken in the coronal third and you can remove it. The worst is when you break the instrument in the coronal third in the early stage and you can not remove it.

Root perforation is a mechanical, iatrogenic, or pathologic communication between the root canal system and the external tooth surface

Weine, Kelly perforation sequence: BLT Perforation :**B**lock your self⇒ **C**reate a ledge⇒ **T**ransportation⇒ **P**erforation.

Ledge: An artificial irregularity created on the surface of the root canal wall that impedes the placement of instruments to the apex of an otherwise patent canal.

Green: The most important factor associated with ledge is root curvature. Size and WL has no effect on producing ledge

Christine M. Sedgley in 2011 (JOE) article compare different root repair materials. Endodontic repair materials are used for various procedures that include pulp capping, apexification, root-end fillings, and perforation repairs. Successful placement of the materials is facilitated by optimal access to the repair site and trouble-free handling properties. Of the repair materials available, mineral trioxide aggregate (MTA) (Dentsply, Tulsa Dental Specialties, Tulsa, OK) possesses several advantageous properties that include good sealing capability, biocompatibility, and antibacterial activity. EndoSequence Root Repair Material (ERRM) (Brasseler USA, Savannah, GA) is a bioceramic material delivered as premixed moldable putty (ESP) or as preloaded syringeable paste (ESS) with delivery tips for intracanal delivery of the material. She found that MTA and ERRM have similar antibacterial efficacy against clinical strains of *E. faecalis*.

Kvinnsland: A combined orthograde and surgical repair of the perforations provided the most favorable outcome with 92%successful. It has been reported that 47% of perforations were noted or created during endodontic treatment, 53% were due to prosthodontic treatment, and that maxillary teeth (74.5%) were more often affected than mandibular teeth (25.5%).

The following questions were answered in Kailing siew (JOE 2015) study:

1) Yet, not many clinical studies that addressed the clinical outcome of repaired root perforations
2) No evidence-based guidelines are available for the most effective way to manage this form of iatrogenic complication that may arise from root canal therapy.
3) For adult patients who had received root canal treatment, does the tooth with repaired root perforation yield a poorer prognosis?

Treatment Outcome of Repaired Root Perforation: A Systematic Review and Meta-analysis: Kailing Siew, Angeline H.C. Lee, Gary S.P. Cheung: JOE: An overall pooled success rate of 72.5% was estimated for nonsurgical repair of root perforations. The use of mineral trioxide aggregate appeared to enhance the success rate to 80.9% but the difference was not statistically significant. The presence of pre-existing radiolucency adjacent to the perforation site fared a lower chance of success after repair ($P < .05$). Maxillary teeth demonstrated a significantly higher success rate compared with their mandibular counterpart ($P < .05$).

Fabio G. Gorni (2016, JOE) assessed the healing outcome of perforations. It was mentioned that with the use of new materials like MTA, the size and the location of the perforation doesn't affect the healing outcome of perforation.

Jew & Weine (1982): Prognosis following perforation dependent upon **time**, **size**, **location** relative to attachment, **salability** of repair material, **diagnosis**. Best prognosis for perf repair is in **apical or middle thirds**. Also **Tsesis (JOE, 2010)** reported that the prognosis of perforated teeth depends on perforation location, perforation size, and time from occurrence.

Sluyk & Hartwell (1998): MTA useful for furcation repair. MTA resisted displacement at 72hr better than 24hr ($p<.05$). No difference if MTA covered by wet or dry cotton pellet (moisture probably derived from furcal tissue). In this in vitro study, found better adapation of MTA to perforation walls when first placed Gelfoam as an internal matrix

Fuss (1996 OOO): Apex locators are more reliable than radiographs for locating root perfs.

Cliff Ruddle (J Caf Dent): Any restorative material within the perforation defect should be removed. The success of treatment for infected perforations depends on removing the contaminants and repairing under aseptic conditions.

Internal Matrix:
Lemon (1992) proposed the internal matrix concept for internal repair of perfs (internal matrix may consist of hydroxyapatitie [Lemon 1992], decalcified FD bone [Hartwell & England 1993], $Ca(OH)_2$ [Petersson 1985] or CollaCote [Rosenberg 1995; IFEA Congress].

Pittford & Torabinejad showed MTA is good for furcal repairs and no internal matrix is indicated under MTA. Also in lateral root perforation cementum was deposited over MTA

Nakata & Baumgartner (1998 JOE): MTA better than amalgam in preventing leakage of F. nucleatum past furcal perf repairs.

Obturation:

Root canal failure is due to poor debridement rather than poor root canal filling (Torneck).

Richert and Dixon 1931: Implanted materials and hollow needle in rabbits. The authors believed that when the tissue of the pulp has been destroyed, it must be filled to the very end in order to prevent "diffusion". Therefore, the filling material must come in contact with the surrounding vital tissue. This filling material must be tolerated by the tissue (biocompatible). The authors also concluded that hollow tubes were not tolerated by the body and therefore, a root canal can not be filled short of the apex. = **"hollow tube" theory** - the idea that the body cannot tolerate an underfilled canal. DISPROVED BY: **Torneck (1967)**: Disproved the hollow tube theory with implanting sterile hollow needles and demonstrating minimal tissue response the body can't tolerate hollow tubes and RCF can't be short. **He proposed that conclusive cause of root canal failure is due to poor debridement rather than poor RCF**. Also **Goldman** disputes the theory.

Klevant 1983 IEJ: Chemo mechanically debrided RC systems of 86 human teeth and left un-obturated for 2 years. Radiographic exam showed significant decrease in PARLs in C&S-unobturated and C&S-obturated teeth. Thus, reject "hollow tube" theory for breakdown of tissue fluid inducing PA lesion. (Should point
out that even though C&S produced significant radiographic healing of AP, better healing was observed in C&S-obturated group.

Mohammad Sabeti (JOE): The noteworthy finding of this study was that there was no difference in healing of apical periodontitis between the instrumented and obturated and instrumented and nonobturated root canal system. **The success of endodontic treatment ultimately depends on the elimination of the microorganism, host response and mechanical closure (coronal seal) of treated root canals that may provide a potential for future bacterial contamination.**

Gutta Percha: 65% ZnO, 20% GP, 10% Opacifier – Barium Sulfate, 5% Wax
Friedman – 65% Zinc oxide (antimicrobial activity); 20% GP; 10% metal sulfates (radiopacity); 5% waxes and resins. According to Friedman the more GP, the stronger and more rigid. ZnO increase the brittleness and decrease the flow.

Goodman & Schilder (1985): 1) GP thermal study: beta to alpha phase at 46-48C and GP in alpha phase to amorphous phase at 56-62C. A small volume reduction occurs when cooling to 37C (so be sure to vertically condense). 2) Compaction not compression happen following GP so there is no spring back ability of GP particles to assist in the sea. 3) Thermal penetration limited to 4-6mm GP.

Senia: sterilize GP by 1min immersion in 5.25% sodium hypochlorite

Kafe, Tamse: Standard radioopacity of GP should be equal to 4 mm aluminum x2 the dentin

Moorer & Genet: Slow and relatively weak antimicrobial effect of GP due to ZO

GP is highly cytotoxic in cell culture experiments, BUT In vivo experiments give a more balanced picture
Sjogren, Sundqvist: Mouse peritoneal macrophages, when exposed to gutta-percha particles, release factors which have a bone resorbing activity that is primarily due to enhanced production of IL-1alpha.

Spangberg (1969): Gutta percha has low tissue toxicity. But REMEMBER that this is due in part to particle size (small GP pieces are extremely inflammatory = **Sjogren** 1995). The raw materials and barium sulfate were not toxic, whereas **zinc oxide and zinc ions showed marked toxicity. All GP points tested were toxic at longer observation periods, and the toxicity was attributed to leakage of zinc ions into the fluids.**

Extruded gutta-percha is associated with delayed healing of the periapex (**Strindberg 1956, Seltzer et al. 1963, Kerekes & Tronstad 1979, Nair et al. 1990b, Sjogren et al. 1990**). Large pieces of gutta-percha are well encapsulated in collagenous capsules, but fine particles of gutta-percha induce an intense, localized tissue response characterized by the presence of macrophages and giant cells (**Sjogren et al. 1995**)

For the first time **Marshal and Massler** proposed the effectiveness of sealer in effective obturation.
Louis Grossman 1976: Ideal Sealer Radioopaque, **Bacteriostatic**, **Adhesive**, **Short setting time**, **Biocompatible**, **Non-staining**, **No Shrinkage**, **Resorbable**, **Soluble in common solvents**, **Hermetic Seal**.

Why use sealer?
Binding agent for RC core filling material
Fills voids and discrepancies in canal walls
Prevents leakage
Acts as lubricant for fill

Grossman's Sealer (Same as **Roth** sealer)
42% ZnO - filler, antimicrobial: **Barkhordar**
27% resin - gives body, coherence, good setting time
15% Bismuth Sub carbonate - accelerates setting time
15% Barium sulfate - radiopacity
1% Borax- retards setting time

EUGENOL: matrix (ZnO-eugenolate), antimicrobial, anti-PLA2, neuromodulator (capsaicin congener)

Sealapex
Base: Ca(OH)2 25%
ZnO 6.5%
Catalyst:
Barium sulfate 18.6%
Titanium dioxide 5%
Zinc stearate 1%

Tubli-seal: ZOE Apexit: Ca(OH)2

Leyhausen JOE: Resin sealers have a long history of use, provide adhesion, and do not contain eugenol. AH-26 is a slow-setting epoxy resin that was found to release formaldehyde when setting. AH Plus is a modified formulation of AH-26 in which formaldehyde is not released. The sealing abilities of AH-26 and AH Plus appear comparable. AH Plus is an epoxy-bis-phenol resin that comes in two tubes.
Powder:
Silver Powder: 10%
Bismuth Oxide: 60%
Hexamethylenentetramine 25%
Titanium Oxide 5%
Liquid:
100% Bisphenoldiglycidyl ether

Spangberg: Talked about cytotoxicity of sealer, proposed that cytotox of ZnOE sealer can be reduced by replacement of eugenol with fatty acids.

Mickel and Wright 1999: compared Roth sealer vs calcium hydroxide (sealapex) showed antimicrobial effect. **Grossman** showed shrinkage of Roths sealer following sealer setting.

Gutmann, Franklin R. Tay (2010, JOE): calcium silicate–based sealer possesses a favorable cytotoxicity profile that was established under extended time periods after setting. The eluent derived from this sealer has comparatively mild toxic effects on the preosteoblast cells when compared with commercially available sealers like AH26 resin based and zinc oxide–eugenol–based sealer (Pulp Canal Sealer) under the same testing conditions. There is also minimal inhibition of the osteogenic potential of the preosteoblast cells. Thus, the experimental sealer may be regarded as minimally tissue irritating even when it is inadvertently extruded through the apical constriction.

Fu-Mei Huang (2010, JOE) suggested that inhibition of alkaline phosphatase (ALP) expression might play an important role in the pathogenesis of root canal sealer–induced periapical bone destruction. They showed that AH26 sealers can significantly reduced the amount of expressed ALP and probably increase the rate of bone destruction following sealer extrusion.

Economides Experimental study of the biocompatibility of four root canal sealers and their influence on the zinc and calcium content of several tissues. J Endod 1995.
Four root canal sealers (AH-26, Roth 811, CRCS, and Sealapex) were tested for tissue biocompatibility in rat connective tissue. Roth 811 and Sealapex caused moderate-to-severe inflammatory reaction, whereas CRCS caused mild to moderate. The most irritant material was AH-26.

Dina B. Gilbert: contamination of prepared root canals with minute quantities of saliva or serum (tissue fluid), together with debris remaining in instrumented canals, may result in a distinct reduction of sealer antimicrobial activity.

Abdulkader 1996: ZnOE sealer had strong antimicrobial activity, then glass ionomer, then calcium hydroxide.

Orstavik 1987, 1988: Zinc oxide sealers are cytotoxic and the effect can be long lasting. Resin based sealer elicit initial severe inflammatory reaction and subsides after.

Augsburger, Peters 1990: Radiographic evaluation of resorption of ZOE sealer/gutta-percha extruded into periradicular tissues. The rate of disappearance of the material did not differ with the presence or absence of radiolucent lesions, type of ZOE sealer used, or obturation technique. **In no case did an irreversible lesion develop where sealer was expressed.** Extruded material did not prevent radiographic repair of radiolucent lesions. Extruded ZOE sealer did not prevent healing of periapical tissues and was removed from apical tissues over the 6 yr follow-up period.

Ricucci and Siqueira (JOE, 2016) do not agree with the previous observation from **Augsburger** which reported that given enough time postoperatively all extruded sealers would be removed. This may be true for the zinc oxide eugenol–based sealers, but only 15% of the AH Plus cases and one third of the Apexit cases showed complete removal of the extruded material in periods longer than 4 years. In the majority of cases in which these sealers were not removed, they remained apparently unchanged on radiographs, even after long periods ranging from 10 years. Also they reported that as for the influence on treatment outcome, there were no statistically significant differences between type of extruded sealers at all follow-up periods and also extrusion of sealer does not affect the healing outcome.

Wicox: Methods of sealer placement: NSD between master cone method, lentulo, MAF

Spangberg (1974): The formaldehyde containing N2 formulation (Sargenti paste) produces extensive tissue necrosis. Since the paraformaldehyde in N2 will not be resorbed, must sx remove Sargenti material expressed beyond apex.

Serper (1998 JOE): Paraformaldehyde pastes are neurotoxic.

Yared GM, Bou Dagher: Displacement of GP apically is more in vertical (1mm) condensation than lateral (o.5mm). They also reported that there is less chance of overextension and less apical leakage in smaller apical preparation (size 25) compared to larger (40) following vertical condensation.

Walton 1981: Less leakage occurs with deeper spreader penetration (w/ in 1 mm, or 2mm w/ master cone), Tug-back is not a good indicator of canal adaptation.

Palamara JE, Messer HH. Load and strain during lateral condensation and vertical root fracture. J Endod 1999: Maximum loads and strains generated by finger spreaders were lower than those generated using a hand spreader (D11T). These loads and strains were also lower than the values at fracture. Lateral condensation alone should not be a direct cause of vertical root fracture.

Brothman 1981 Vertical compaction demonstrated **TWICE** the number of lateral and accessory canals and denser fill.

Freidman (Toronto study phase 3): 89% total success for Warm vertical condensation FPVC: Flared preparation / vertical compaction. 73% total success for Lateral condensation SBLC: Step Back Lateral Compaction

Bumbgartner: There is NSD in the apical leakage between vertical and lateral condensation. However, thermafill leaked the most due to stripping the carrier.

Also **Reader** said NSD in the apical leakage between vertical and lateral condensation. However, vertical will fill the lateral canals and can shows the anatomy better.

ElDeeb, Zucker: Both linear and volumetric leakage correlates with the obturation density especially in middle third of root **Also Byer-Oslen reported root canal treated teeth with homogenous obturation might not leak but vise versa is not correct.**

Schaeffer, White, Walton, 2005 JOE (Harward, Meta-Analysis of literature) Obturating materials extruding beyond the radiographic apex correlated with a decreased prognosis. A better success rate is achieved when treatment includes obturation short of the apex > 1mm compared to over filled.

Sami Chugal, Spangberg 2003: presence of chronic apical periodontitis, level of filling and density of filling affects the outcome.

Allard & Stromberg 1987: Dog study: In microbiologically-induced PA lesions, got 4 month healing even when obturate with bacteria remaining in canal systems. (**Contrast with Sjogren 1997 who showed in humans that prognosis is reduced if bacteria are present at time of obturation)** We can also reject the Sjogren study by **Delivanis & Mendel (JOE-1983)** that organisms are not capable of survival inside obturated root canal for a long time

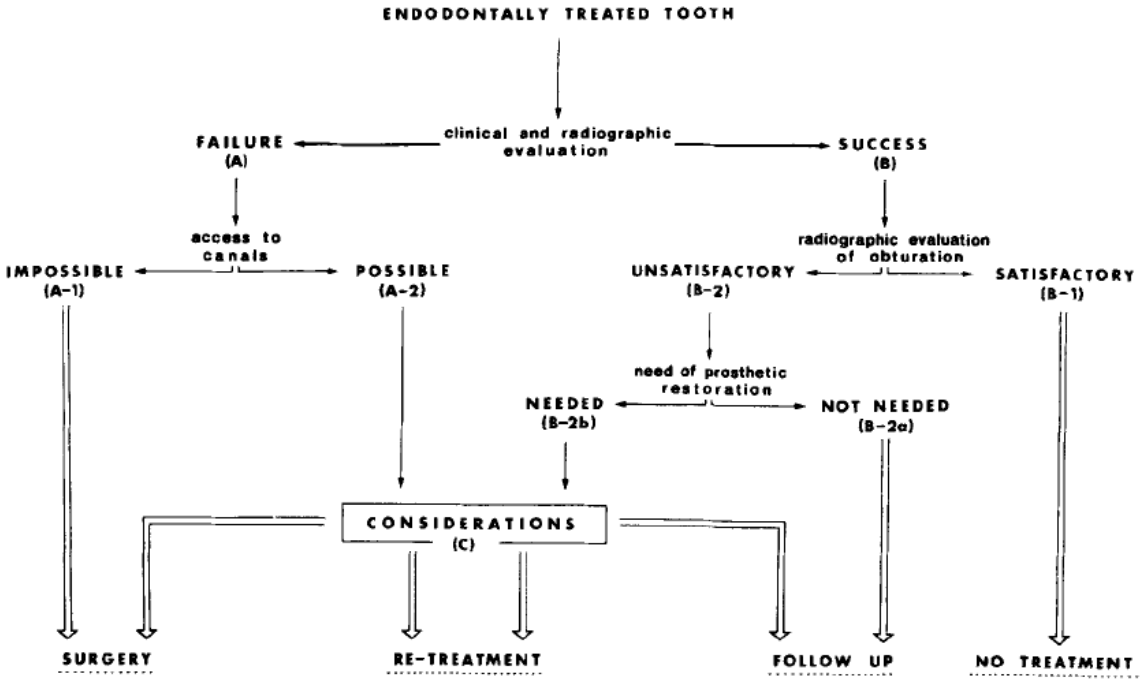
Baumgartner JC: Incidence of pain associated with clinical factors during and after root canal therapy. Part 2. Postobturation pain. J Endod 1983. Extrusion of sealer or gutta-percha was associated with increased pain. Overall incidence of postobturation pain was 47.6%.

Gutmann: 10 degrees C temp change will damage the PDL cells; temps never reached this high. However, **Baumgartner J Endod 2001** showed that at no time did the System B, the Obtura II, or ultrasonic delivery of warm gutta-percha exceed an increase of 10 degrees C at any thermocouple level on the external root surface.

Cohen G. Pulp response to externally applied heat. **Oral Surg Oral Med Oral Pathol 1965.**
Monkey study. Temp increases (C) had these effects:
4 degrees- pulps recovered
10 degrees- 85% recovered; 15% necrotic
20 degrees- 40% recovered; 60% necrotic
>20 degrees- none recovered

Retreatment

Stabholz & Friedman: Before doing re-tx there are couple of questions you should ask: 1) Is it worth damaging a successful restoration in order to gain access to the root canals? 2) Is it necessary to retreat a case just because it seems radiographically unsatisfactory and 3) what are the chances of improving the filling by retreatment? 4) What are the chances of success in cases where previous treatments failed, especially when no apparent reason can be suggested for failure?



Stabholz & Friedman strategies for Re-treatments:

1) In case of non properly filled cases you can use hand files to remove the gutta percha.

2) The more condensed the root filling, the more difficult it is to remove it.

3) Restorations of poor quality, particularly those with poor marginal adaptation or secondary caries, should be removed for retreatment to be later remade. A satisfactory restoration should be retained, being either perforated, with subsequent repair, or removed, with subsequent re-cementation.

4) In curved roots the gutta percha should be dissolved to allow resistance-free negotiation of the curves and prevent ledging or perforating the root canal. In straight roots gutta-percha can be removed with rotary endodontic instrumentation.

5) In root canals that were prepared and filled considerably short of their apices, particularly the curved ones, it should be assumed that ledges may have formed at the apical end of the preparation. To prevent carrying the ledges further in such cases, forceful removal of the gutta-percha should be avoided and it should be dissolved

6) Coronal ends of silver cones that extend into the pulp chamber should be preserved and used as handles to pull out the cones. They are visible in radiographs, except with amalgam cores. You can use grasping pliers (**steiglitz**), file and solvent and indirect ultrasonic.

7) In removing hard cement use ultrasonic and vibration or drilling with surgical bur half round bur

8) Dissolving gutta-percha is advocated whenever it is well condensed and in curved roots, particularly when the obturation terminates short of the apex and at the curve

9) The use of solvents eliminates the need for excessive force during the negotiation of the gutta-percha obturated canals. Such force can lead to undesired transportation of the canal space.

10) Removal of gutta-percha with rotary instruments is indicated only in straight canals and those in which the gutta-percha appears to be well condensed.

11) The removal of the material should not result in a change in the canal morphology, so that the objectives of endodontic therapy can be maintained.

Allen, Newton and Brown (1979): The overall success rate for retreatment was 65.6% with an additional category of "uncertain" of 18.3%. Surgical treatment was necessary to retreat 53.5% of the cases. pastes, semi-solid materials (gutta-percha), and solid materials (silver cones and broken instruments) constituted 20.6%, 53.6%, and 21.7%, respectively in re-tx cases.

Gorni and gagliani: Although the overall success was 69.03%, the success in the root-canal-morphology-respected group was 86.8% and in the root-canal-morphology-altered group 47%. **The clinical success of an endodontic retreatment seems to depend on whether alterations in the natural course of the root canals were caused by previous root-canal treatment.**

Success of Re-Tx (**Molvern & Halse 1988; Sjogren 1990 and Frideman 1995**)
No PARL: 89-100%
PARL: 56-71%

Bergenholtz (1979 Scan JDR): Group being re-tx for **prosthetic indication** (ie, not failing) still had 6% failure rate

Allen (1989 JOE): Retrospective study of 1,300 cases. 65% success 16% uncertain. NSRCT Re-tx better success than sx (73% vs 57%).

Sjogren (1990): Re-tx teeth with AP has 62% success rate

Moiseiwitsch & Trope (1998): Re-tx is preferable over endo sx

The highest rate of success in retreatment cases is when the failure is due to missed canals which can be cleaned and shaped

Chong and Pittford: **Appropriate case selection** for retreatment can increase the success rate of Re-tx.

Thermafil is an endodontic obturator consisting of a solid carrier coated with alpha-phase gutta-percha. After heat softening the gutta-percha and inserting into the root canal, the carrier is sectioned and becomes

incorporated into the gutta-percha. The carrier was originally made of metal, but plastic carriers are used in the current product (Thermafil Plus; Dentsply Tulsa Dental, Tulsa, OK).

Ibarrola: removal of thermafill in retreatment cases is easy using K file and chloroform. **Wilcox & Juhlin:** It may be prudent to use mechanical means to remove as much of the Thermafll gutta-percha as possible before a solvent is used in retreatment.

Tatsuya Hayakawa (JOE, 2010): ProTaper Retreatment Files are useful for removing Thermafil Plus plastic carriers. Among them, the D1 instrument has an active cutting tip that facilitates initial penetration into a gutta-percha filling. The greater taper of this instrument (9%) may also facilitate prompt binding to the carrier and canal wall. These design features may favor efficient removal of the carrier. It was also suggested that removal of carrier is easier in cases with smaller tip and taper.

Silver points are soft and they should not be touched directly with ultrasonic. **Seltzer** confirmed corrosion products of silver amin sulfate which is cytotoxic in retreatment cases.

Abramovitz (JOE): Posts shorter than 5 mm are not usually considered obstacles for Endo re-treatment.

Gaffney JL, Lehman JW: It has been suggested that the application of ultrasonic vibration to a post would weaken its retention, facilitating its removal in re-treatment cases.

Removing GP: **Ultrasonic**, **Safe End Burs**, **Touch and Heat**, **Retreatment files**, **Chloroform**. Try to remove the GP mechanically before using chloroform. Using chloroform following 1 ml syringe technique (Donnelly) After adding chloroform use paper point to resorb the dissolved GP.

Tamse (1986): GP Solvents: chloroform > xylene >> Endosolv-E (Tetrachloroethylene) > orange turpene oil, Halothen, eucalyptol.

Hartwell GR, Moon PC. The effect of endodontic solutions on resorcinol-formalin paste. J Endod 2003. This study determined if 0.9% sodium chloride, 5.25% sodium hypochlorite, chloroform, or Endosolv R would have a softening effect on resorcinol-formalin (red Russian= Resorcinol-formaldehyde resin is a material used in endodontic therapy in many foreign countries. It contains two potentially toxic components, formaldehyde (liquid) and resorcinol (powder)). Sodium hypochlorite was superior to all other groups after 5 min.

Carpenter (JOE, 2014) showed the efficacy of chloroform in dissolving MTA based sealers like MTA Fillapex and regaining patency in retreatment cases filled with MTA sealers.

Wilcox (1987 & 1989 JOE): Examined RC walls after heat, files, chloroform, US for Roths 801 vs AH26. All techniques incompletely cleaned walls; AH26 more difficult to remove than Roths.

Wilcox J Endod 1991: Since re-instrumented canals usually enlarge in the same direction as the first instrumentation, retreating one's own failure is unlikely to debride areas previously undebrided. if you go to the same angle you won't fix the problem in the retreatment and always try to get straight line access.

Kaplowitz GJ. Evaluation of Gutta-percha solvents. J Endod 1990. Five solvents (rectified white turpentine, oil of melaleuca, eucalyptol, white pine oil, and pine needle oil) were compared with chloroform for their ability to dissolve gutta-percha. All solvents dissolved at least 50% of the gutta-percha, and chloroform dissolved the gutta-percha completely.

Hansen MG. Relative efficiency of solvents used in endodontics. J Endod 1998: Eucalyptol, eucalyptus oil, orange oil, chloroform, and xylene were used to remove gutta-percha and several different types of sealers. Only chloroform removed AH-26.

Metzger Z, Removal of overextended gutta-percha root canal fillings in endodontic failure cases. J Endod 1995. A procedure for the removal of an overextended root canal filling is presented. First, the gutta-percha is softened and removed to a distance of 2 to 3 mm short of the apex. Second, the remaining gutta percha is removed by a Hedstrom file. The file is extended 0.5 to 1.0 mm beyond the apex, firmly engages the gutta-percha and is slowly removed.

Chutich MJ: Risk assessment of the toxicity of solvents of gutta-percha used in endodontic retreatment. Compared chloroform, xylene, or halothane and it is proposed that the use of any of the aforementioned solvents used in the retreatment of root canals would pose negligible risk to the patient.

Mcdonald: Air vapor of chloroform is below the toxic level and chloroform is safe.

Baumgartner JC: Use of chloroform during endodontic retreatment significantly reduced intracanal levels of cultivatable E. faecalis.

Retreatment in asymptomatic teeth?? Is it cost effective?
Decision-making for clinically asymptomatic, endodontically treated teeth with radiographic findings such as underextended or overextended fillings or periapical lesions introduces uncertainty and often leads to variability of the made decisions. On the one hand, it seems that only a minority of radiographic failures translate into clinical failures and the need to retreat whereas it is advocated that retreatment is required and suitable to mend radiographic imperfections or allow resolution of periapical lesions. Prediction of disease progression or exacerbation in teeth with such findings is difficult and many outcomes used for assessing the "success" of initial and retreatments are defined by professionals, not patients who might prioritize other parameters. Dentists often understand re-treating teeth with insufficient root fillings or periapical lesions as their professional duty, whereas patients might prefer to not re-intervene as long as there is no subjective need and the option for retreatment remains. Clinical decision-making should integrate both professional and lay judgment and preferences and should also consider the consequences emanating from each treatment decision. **Falk Schwendicke study (JOE, 2015)** aimed at evaluating the long-term cost-effectiveness of both strategies. In contrast to what was described above, analysis did not find a decision dilemma, because cost differences between strategies were high, and the advantages of performing immediate retreatment were limited or absent in the majority of scenarios. **On the basis of results, retreating clinically asymptomatic teeth with one of the described radiographic findings was usually not cost-effective**

Anatomy:

Anatomy of Teeth-who and how they studied them

Authors	**Type of Study**
Vertucci	Clearing and dye
Pineda and Kuttler	Radiographic
Caliskan	Clearing
Kasahara	Clearing
Todd	Clinical
Carns and Skidmore	Plastic cast resin
Kerekes and Tronstad	Ground sections
Green	Ground sections and microscope
Acosta el al	Ground sections and magnification
Gopikrishna	Clinical (spiral computed tomography)
Seidberg	Sectioning
Stropko	Clinical (microscope)
Weine	Radiographs (with files)
Gilles and Reader	SEM and microscope
Pomeranz and Fishelberg	Clearing
Kulild and Peters	In vitro (microscope)
Benjamin and Dowson	Radiographic with files
Lu	Radiographs and sectioning
Baisden	Serial sections
Ricucci	Clinical
Carns and Bjorndal	Cast resin
Hess	Vulcanite Rubber
Plotino	MicroCT
Bellizi and Hartwell	Radiographic evaluation

Maxillary Central Incisors:

- Vertucci 100% one canal
- Todd: two canals case report

Maxillary Lateral Incisors:

- Chohayeb 52% distopalatal inclination, 15% labially, 8% distally, 2% straight

Maxillary Canine:

- Caliskan 2.2% two canals

Maxillary First Premolar:

- Vertucci 69% two canals
- Bellizzi & Hartwell 91% two canals, 6% one canal and 3% three canals
- Muller 98% two canals

Maxillary Second Premolar:

- Vertucci 33% two canal
- Bellizzi & Hartwell 59% two canals, 40% one canal, 1% three canals
- Pineda & Kutler 45% 2 canals

Maxillary First Molar:

- Kulild & Peters: 95% 4 canals that 54% located by hand, 31.3 by burs.
- Stropko: 93% 4 canals
- Gilles & Reader: 90% 4 canals
- Weine: 50% have 4 canals. 35% Type 2 and 15% Type 1.
- Vertucci 55% 4 canals
- Benenati case reported maxillary molar with 2 palatal canals
- Peikoff & Christie showed maxillary molar with 2 palatal canals happen every 3 years (0.4%) with the same prognosis

Maxillary Second Molar:

- Gilles & Reader: 70% 4 canals
- Weine: 40.3% 4 canals
- Stropko 67% 4 canals
- Pomeranz 69% 4 canals
- Vertucci 29%

Mandibular Incisors:

- Benjamin & Dowson: 41% (type II) had two canals but only 1% were type III
- Vertucci: 30 – 25 – 22 % (two canals) in central, incisor and canine (22% in no. 22)

Mandibular First Premolar:

- Vertucci 25% two canals – one in four!
- Zillich & Dowson 23% 2 canals
- Trope, Elfenbein and Tronstad – 40% African American will have two or more.
- Kulid & Baisdem if there are 20 canals it is most probably type 4.

Mandibular Second Premolar:

- Vertucci 2.5% two canals, 98% one canal
- Zillich & Dowson: 12% two canals, 0.4% three canals, 84% one canal
- 25% of mandibular PM with two canals are type 4.

Mandibular First Molar:

- Bellizzi & Hartwell: 35% four canals
- Fabra-Campos: 48% four canals

- Vertucci: 28% - at least one in four!
- Bjorondal and Skidmore 28.5% four canals
- Pineda & Kuttler: 27% four canals

Mandibular Second Molar:

- Bellizzi & Hartwell: 5.5% four canals
- Pineda & Kuttler: 5.6% 4 canals
- Vertucci: 7% 4 canals

It has been reported that older ages (ie, 51–70 years) are associated with fewer MB2 canals **(Reis, 2013).**

2010 (JOE) study by Valencia de Pablo was a systematic review regarding the root Anatomy and Canal Configuration of the Permanent Mandibular. It was stated that the incidence of a third root was 13% and was strongly correlated with the ethnicity of the studied population. Three canals were present in 61.3%, 4 canals in 35.7%, and 5 canals in approximately 1%. Root canal configuration of the mesial root revealed 2 canals in 94.4% and 3 canals in 2.3%. The most common canal system configuration was Vertucci type IV (52.3%), followed by type II (35%). Root canal configuration of the distal root revealed type I configuration in 62.7%, followed by types II (14.5%) and IV (12.4%). The presence of isthmus communications averaged 54.8% on the mesial and 20.2% on the distal root.

Kartal: MB canals of the mandibular molars have the highest rate of primary curvature

Gutmann JL: Prevalence, location, and patency of accessory canals in the furcation region of permanent molars. Accessory canals were demonstrated in the "furcation region" in 28.4% of the total samples of molars; 29.4% in mandibular molars, and 27.4% in maxillary molars.

C- Shaped Canals:

- Newton & McDonald: found C-shaped canals in Maxillary First Molar
- Cooke & Cox: 8% C-shaped canals in Mandibular Molars (2^{nd} & 3^{rd}) they said it is hard to anasthetis and bleeding
- Weine: 7.6% in mandibular molar. It is more common in young patient
- Gilbert & Rice: C-shaped in Mandibular Molars (went downstairs)
- Simon talked about radiographic detection of C shape: 1) Root appear conical and fused 2) long pulp chamber 3) pulp chamber is indistinct as it goes apically 4) little or no furcation
- Jafarzadeh 2007 JOE: Semi colon is the most common type of C shape canal (ML is separate and the MB and D join) lots of bleeding, hard to get numb,

Middle Mesial Canal:

- Pomeranz: 12% MM; 8 Fins, 2 Confluent and 2 Independent
- Fabra-Campos: 2% MM (5 canals)
- Ali Nosrat (JOE, 2015) 20% and it is more common in young patients. Under 20= 32.1%(1 in 3) 20-40= 23.8% (1 in 4) over 40=3.8%
- Azim: 46% MM
- Jacobson= if there is a sulcus between mesial canals should be probed for additional canals. Any sign of persistent pain, bleeding and lesion on mesial canal can be indicator of MM

Bone & Moule: 85% of palatal roots curved >10 degrees to the buccal side. S-shaped (Bayonet) Palatal canal 13% in first molar and 25% in second molar.

Ferraz: Radix Entomolaris: Asian population. Mongolian (the presence of additional distolingual root)

Sabala, Benenati: Most aberrations are bilateral (60%). Most common is bifurcation in mandibular PM. Least is seen in anterior maxillary.

Radicular lingual groove:

1) **Peikoff & perry**: poor prognosis
2) **Withrs:** incidence of lingual groove (94% in max lateral and 2.3 % in central)
3) Goon, Carpenter: The groove is covered with cellular cementum. The dentin near the base is dysplastic and communicate with pulp. The formation of grove is due to in folding enamel epi and Hertwigs. prevalence < 3%

Dens Invaginatos:

1) **Hovland & Block**: Incidence 0.04-10% detecting using angled film
2) **Desmit & Demaut** elaborated different types 1) confined in crown and above CEJ 2) extend below CEJ 3) extend below CEJ and reach perio membrane 4) extend below CEJ and reach apex

Dens evanginatus :

1) **Priddy&Regezi**: Is an rare anomaly on PM covered with enamel and contain pulp horn (due to proliferation of ameloblast layer. More common in Mongolia

2) **Chen:** Most common on mandibular 2 PM. Teeth with necrotic pulp treated with Ca(OH) and vital teeth were treated by 6 months interval grinding and treatment with Sn-F.

	Distance from apex to foramen	**deviation**
Green (ant)	0.2- 0.3	63%
Green (pos)	2mm	50%
Levy and Glad	0.2	66.4%
Pineda, Kuttler	2-3mm	83%

Vertucci: Position of apical foramen (in all teeth) was 80% to lateral rather than central

Burch, Hulen: 92.4% of canal foramina did not exit at the anatomic apex (Average deviation was 0.59 from apex)

Stein TJ, Corcoran JF: There is a positive correlation, which could not have occurred by chance that as age increase the deviation and the width of the foramen opening both increase due to cementum deposition and apex thickening by age.

Morphology of the Physiological Foramen: I. Maxillary and Mandibular Molars: **Benjamín Briseño Marroquín**. All apical size constriction are below 300 micro except distal of lower molar. The most common configuration is Oval

Vertucci: 74% of accessory canals cases they are found in the apical third of the root, in 11% in the middle third, and in 15% in the cervical third. Accessory canals contain connective tissue and vessels but do not supply the pulp with sufficient circulation to form a collateral source of blood flow

Access:

Krasner and Rankow: Anatomy of the Pulp Chamber Floor 2004: Laws of symmetry, law of color change and Law of CEJ

The following observations were noted relative to all teeth:

1. The floor of pulp chamber is always a darker color than the surrounding dentinal walls
2. This color difference creates a distinct junction where the walls and the floor of the pulp chamber meet
3. The orifices of the root canals are always located at the junction of the walls and floor
4. The orifices of the root canals are located at the angles in the floor wall junction
5. The orifices lay at the terminus of developmental root fusion lines, if present
6. The developmental root fusion lines are darker than the floor color
7. Reparative dentin or calcifications are lighter than the pulp chamber floor and often obscure it and the orifices.

The following observations were noted relative to all teeth except maxillary molars:

1. If a line is drawn in a mesial-distal direction across the center of the floor of the pulp chamber, the orifices of the canals on either side of the line are equidistant.
2. If a line is drawn in a mesial-distal direction across the center of the floor of the pulp chamber, the orifices of the canals on either side are perpendicular to it.

These observations were consistent enough that several anatomic laws regarding the pulp chamber floor can now be proposed:
Law of symmetry 1: except for maxillary molars, the orifices of the canals are equidistant from a line drawn in a mesial distal direction through the pulp-chamber floor.
Law of symmetry 2: except for the maxillary molars, the orifices of the canals lie on a line perpendicular to a line drawn in a mesial-distal direction across the center of the floor of the pulp chamber.
Law of Color Change: the color of the pulp-chamber floor is always darker than the walls.
Law of orifice location 1: the orifices of the root canals are always located at the junction of the walls and the floor.
Law of orifice location 2: the orifices of the root canals are located at the angles in the floor-wall junction.
Law of orifice location 3: the orifices of the root canals are located at the terminus of the root developmental fusion lines.

Wilcox and Walton talked about the orifice location patterns:

- Orifice locations tend to be centered occlusaly (i.e does not go toward M.R)
- Max molar->
    - MB orifice was never mesial to the lingual triangular ridge of the MB cusp
    - MB orifice generally half way between the LTR and Central groove.
    - DB orifice slightly distal to the buccal grove.
    - Palatal orifice slightly distal and buccal to ML cusp.
- Mand molar->
    - MB orifice was on or distal to the LTR but never mesial to MB cusp
    - ML orifice was on or just lingual to the central groove and slightly distal to MB orifice.
    - D canal, just buccal to to the central groove.

Adham Azim investigated the anatomic landmarks which are useful in accessing maxillary and mandibular teeth using CBCT (JOE, 2014).

Teeth		(cusp to pulp chamber ceiling)	(cusp to pulp chamber floor)	(cusp to coronal furcation)	(cusp to apical furcation)	(pulp chamber floor to furcation)	(pulp chamber ceiling to furcation)	(pulp chamber height)
Maxillary molar	Mean	6.54	8.66	10.63	11.19	1.97	4.09	2.12
Mandibular molar	Mean	6.38	7.92	10.16	10.36	2.24	3.78	1.53

Numbers are in mm

Krishan (JOE, 2014): Although **conservative endo cavity (CEC)** was associated with the risk of compromised canal instrumentation only in the molar distal canals, it conserved coronal dentin in the 3 tooth types and conveyed a benefit of increased fracture resistance in mandibular molars and premolars (x2).

Goodman: Suggested to start the access with round bur

Day 1975: Use of **Endo Z in unroofing.** Rankow talked about access box and importance of **unroofing.**

Leeb 1983: Remove the **DENTINAL TRIANGLE** or cervical ledge near the orifice (straight line access)

Teplitsky & Sutherland: Access through crown with diamond bur was more effective. In access preparation in PFM first use diamond to get in porcelain and then change to carbide in metal.

McMullen: Endo access can reduce the retention of PFM crown on anterior teeth by 60%. However, this is not true for posteriors because the access is not parallel to the long access. The retention of crown can be gained or even surpass following restoring the access using amalgam.

Apex locator:

Suzuki reported that PDL and mucosa have an electrical resistance in dug. **Sunada** applied it in humans to develop the apex locators.

Kobayashi (New electronic canal measuring device based on the ratio methodJ Endod, 20 (1994): The most striking disadvantage of most apex locators is that if there are electrolytes in the canal the meter shows a reading which is too short or sometimes the measurement itself becomes impossible. To overcome this drawback, a new concept for electrically measuring the root canal length has been developed. The device simultaneously measures two impedances of the canal using current sources with two different frequencies. Then the ratio between the two electric potentials proportional to each impedance is calculated. The quotient is shown on the device's meter and represents the position of a file tip in the canal. The present study found that the quotient was only negligibly influenced by the electrolyte present in the canal and decreased considerably as the file tip approached the apical foramen. Developed the ROOT ZX
Root ZX measures impedance at 8 and 0.4kHz frequencies, and calculates a quotient of the impedances.

Fuss (1996): Describes use of Apex Locators to locate perforations.

Beach & Hutter 1996: Case report of using apex locator on a pt with a pacemaker

Fouad: Fluids cause less accurate and shorter reading. Naocl and blood had the most significant effect. The highest inaccuracy in apex locator reading occurred in case with open apex and flooded with Naocl.

Schilder: The following irrigants were tested: 2% lidocaine with 1:100,000 epi, 5.25% NaOCl, RC Prep, liquid EDTA, 3% H2O2, and Peridex. Results: The Root ZX EAL reliably measured canal lengths to within 0.31 mm and there was no difference in the length determination as a function of the seven irrigants used.

Goldberg: Root ZX may be used accurately to determine working length in teeth with apical root resorption.

Huang (JOE): Two factors affect the accuracy of the apex locator: **moisture** and the **diameter of the apical foramen**. Root canal should be kept dry. In case of bleeding and inflammation postpone the reading

Foad, Krell: variability in the apex locator.Therefore, we should verify the WL after apex locator with radiographs Also **Brunton** said that the apical foramen was more accurately located with combination of EAL and radiographs.

Mayeda (1993): There is no difference in the reading of apex locator in vital and necrotic cases,

Rivara: Instrumentation caused 0.63mm reduction in working length reading using apex locator. Recapitulation was necessary to obtain length-reading with apex locator.

Shabahang: Accuracy of apex locator (root ZX) around 96.4%. Always remember to turn on the apex locator before you connect it to file.

Fouad (1993): Apex locaters ok on pts with a pacemaker

Finally, are apex locators reliable? Jorge N.R. Martins (JOE, 2014) performed a Meta analysis to to compare the radiographic and electronic methods. It was concluded that the apical locator reduces the patient radiation exposure and also that the electronic method may perform better on the working length

determination. **At least one radiographic control should be performed to detect possible errors of the electronic devices.**