

Endodontics, the name derived from 'Endo' means inside, 'Dont' means the tooth and 'ics' means the study; that is, the study of inside of the teeth. The pulp, which is inside the tooth, is a specialized connective tissue encased by dentin. The dentin is further covered by enamel in the coronal part and cementum in the radicular part. The collective study of physiology and pathology of pulpal tissue along with their sequalae is 'Endodontics'.

DEFINITIONS

The science dealing with diseases of pulp and the periapical tissues is endodontics. It is defined as 'the division of dental science that deals with etiology, diagnosis, treatment and prevention of diseases of dental pulp and their sequelae'.

SCOPE OF ENDODONTICS

Pulpal and periapical diseases are common in dentistry. Untreated cases lead to bone destruction and subsequent extraction of the concerned tooth. Endodontics provides treatment to such cases and the tooth can be saved; protecting stomatognathic system in functions. Endodontics can be beneficial in variety of cases, such as:

- Pulp exposures (complete or partial)
- Periapical abscess
- Root fractures
- Root perforations
- Teeth with incomplete apical root development
- Endodontic implants
- Replants
- Transplants (autotransplants or allotransplant)
- Occlusal trauma causing reversible pulpitis
- Overzealous root planing and curettage, leading to pulpal sensitivity
- Extensive infrabony pocket formation extending beyond the root apex

- Surgical intervention of pulpal problems (apicoectomy, hemisection, etc.)
- Developmental anomalies of pulpal tissue.

EVOLUTION OF ENDODONTICS

The evolution of scientific development in endodontics dates from the third decade of 17th century. Literature on the early history of endodontics is sparse and undocumented as early history of dentistry. The beginning of endodontics is both slow and late. It was further retarded by the focal infection theory. Only in 1956, it attained a degree of acceptability and respect when the American Board of Endodontics was established.

An archaeological excavation by the department of antiquities and museums in northern Negev desert (Israel) recovered the skeletal remains of 25 people buried in a mass grave approximately in 200 BC. Subsequent analysis of the dentition showed one skeleton with a 2.5 mm bronze wire implanted in maxillary right lateral incisor. This is the first archaeological evidence of endodontic procedure performed in ancient Israel, which is documented.

On the radiograph, the root canal appears to have been artificially widened to a depth of 2.5 mm in preparation for insertion of the wire. This implies direct intervention by a skilled dental practitioner rather than a haphazard procedure performed by a layman.

The pulp of an aching tooth was often cauterized either by a red-hot cautery or by means of a chemical or a weak acid. The use of a hot wire has been mentioned by F. Hoffman (1753) in his book *A Treatise on the Teeth; their Disorders and Cure*.

Josiah Flagg of Boston, the first American to practice dentistry exclusively, relieved pain of an abscessed tooth by creating an opening into the crown, leading to the pulp cavity. He named this operation as 'tapping the pulp'.

Although the pulp was left to die by cauterization, or intentionally devitalized by heat or chemicals; its intentional removal was not planned until 1824 when Delmond of Paris devised a fine, hooked instrument for that purpose. The removal of the pulp was less painful and effective with this instrument.

In 1838, Edwin Maynard took a watch spring and filed it down to make a four-sided broach, which can entwine and remove the pulp easily. Robert Arthur cut barbs on broaches with a penknife in 1853. In 1885, the Gates Glidden drill and in 1904, the K-file were introduced. Standardization of instruments was proposed by Trebitsch in 1929 and again by Ingle in 1958 but again meant to be reviewed for rotary Ni-Ti instruments.

Following removal of the entire pulp, radicular space preparation was done by step-back or telescopic technique since 1969 as first described by Clem and Weine. Another major breakthrough for root canal preparation as crown down technique was given by John Pappin and Marshall in 1980, followed by "Balanced force" concept by Roane in 1985.

Philip Pfaff performed the conventional pulp capping of diseased pulp in 1756. In 1874, Adolf Witzed of Germany tried pulp mummification with different materials. In 1836, in "Guide to sound Teeth", Shearjashub Spooner introduced a technique for pulp devitalization of the pulp by arsenic. This technique continued for well over 100 years. Chapin A. Harris of Baltimore, one of the founders of the first dental school, who also used the drug at the same time; however, he warned against its use because of arsenic potential to damage the teeth and soft tissue. About the middle of the 19th century, efforts were made to conserve the pulp with medicaments such as creosote, Canada balsam and alcohol. The agent used was wiped over the exposed pulp and it was capped with metal disk, oiled silk, asbestos, plaster of Paris, lead or tin foil, collodion, etc.

Root canal filling actually preceded removal of the entire pulp. After the removal of the pulp, the canal was filled with some foreign substance often gold foil. Documentary proof of gold foil fillings in 1809 by Edward Hudson of Philadelphia is available. In 1890, Gramm used copper points, which were plated with gold to prevent dissolution.

Guttapercha, an extract of trees of sapodilla family, mixed with lime, quartz and feldspar; was introduced in 1850 and marketed under the name of Hill's stopping. In 1867, GA Bowman of St. Louis used guttapercha points for filling of root canals.

Working length determination was performed by radiographic technique since 1908 as first described by Meyer L. Rhein. In 1918, Custer for the first time reported use of electric current to measure root canal working length. Eventually Sunada in 1962 introduced electronic apex locators.

In early 1930's, silver cones were introduced for filling root canals by H. Trebitsch and later modified by E. Jasper of St. Louis.

The first cement was used in dentistry in 1856. A crude composition of zinc oxide and a solution of zinc chloride known as oxychloride of zinc was popular at that time.

Two outstanding English dentists, John Hunter, who wrote, 'The Natural History of Human Teeth (1778)', and Joseph Fox strongly advocated transplantation of tooth. Hunter used to boil the teeth before transplantation. Since venereal diseases were rampant, boiling of teeth was preferred. However, it was not done for reasons of sterility but rather for removal of the attached soft tissue. Hunter first successfully implanted a human tooth in a cock's comb.

James Gardette, (1950) another Philadelphia dentist, is given credit for intentional replantation of teeth in America.

In 1864, Stanford C. Barnum of New York invented rubber dam for keeping the operative field clear of saliva and soft tissues.

Otto Walkoff in 1891 introduced camphorated monochlorophenol as an intracanal medicament, which he found to be more effective and less irritating.

Wilhelm Konrad Roentgen discovered X-ray in 1895. Two weeks after Roentgen announced his discovery, a pioneer in endodontics, Professor Otto Walkhoff, took radiograph of his own teeth, exposing the plate for 25 minutes.

In 1906, Dr John P Buckley mixed cresol with formalin, which became known as Formocresol, and is still the favoured intracanal medicament among practising endodontists.

Until the late 1850s, ice and heat had been used to determine whether the pulp was dead or alive. In 1867, Magitot of France, suggested the use of an electric current to determine if vitality was present in a tooth. However, Marshall in 1891 popularized it. Focal infection theory promulgated by William Hunter in 1910 was blindly followed in dentistry, particularly in root canal treatment.

Local anesthesia was discovered in 1884, when at the suggestion of Sigmund Freud; Carl Koller, a Viennese ophthalmologist, first used a solution of cocaine as a topical anesthetic for eye surgery. In 1885, William S. Halsted of New York, made the first block injection (a mandibular bone) with the cocaine solution. Myer in 1904 developed 'Myer Dental Obtunder' a high-pressure syringe for anesthetizing the pulp and in 1906 infiltration anesthesia was introduced by Vaughan.

The placement of calcium hydroxide as a sub-base in deep cavities where the removal of all decay would expose the pulp (indirect pulp capping) has been used successfully since its introduction by Walter Hess in 1951.

Numerous agents are being used for smear layer removal from the root canals, like EDTA (15% Ethylenediaminetetraacetate acid) since 1957 by Nygaard-Ostby followed by Fehr in 1963 who introduced EDTAC (15% EDTA + Cetrimide) and Steward 1969 RC Prep (10% urea peroxide + 15% EDTA). Citric acid in 40% concentration was first used by Tidmarsh in 1978 followed by 20% concentration by Wayman (1979) and 10% citric acid by Baugmgartner (1984). Koskinen reported the success of several cases using Tubulicid (38% benzalkonium chloride, EDTA, 50% citric acid) in 1975 followed by Largal Ultra (15%

EDTA, Cetrimide, NaOH) in 1980. Salvizol another root canal chelating agent with broad spectrum bactericidal activity (5.0% aminoquinaldinium diacetate) was introduced by Kaufman in 1981. Torabinejad first used MTAD containing citric acid and doxycycline as decalcifying substances in 2003.

The period of dentistry in the early part of 20th century was characterized by the introduction of basic sciences, especially Endodontics. As we go back to 200 years of progress in endodontics, it is almost like comparing the stone age with the present technologies (Table 1.1). Various sciences have contributed to a much better understanding of the physiology and pathology of pulp, enabling us to examine and compare it in health and disease.

Table 1.1	Evolution of Endodontics
200 BC	First evidence of endodontic dentistry with 2.5 mm bronze wire in maxillary right lateral incisor
500 AD	Aetius first recorded endodontic surgical procedure (the incision and drainage of an acute abscess)
1725	Lazare Riviere used clove oil as obtundent, later used oil of cinnamon, camphor or turpentine
1728	Pierre Fauchard in his textbook "Le Chirurgien Dentiste" first described dental pulp
1746	Pierre Fauchard described removal of pulp
1753	F. Hoffman advocated cauterization of pulp with hot wire
1756	Philip Pfaff described pulp capping of diseased pulp
1757	Bourdet described a therapy of extracting carious teeth, followed by filling the canals with gold and re-implanting them
1778	John Hunter advocated re-implantation when crown was partially destroyed due to caries
1783	Woofendale used cautery for destroying the pulp to relieve pain
1809	Edward Hudson plugged root canal with gold foil in anterior teeth only
1820	Leonard Koecker used hot wire for cauterization of exposed pulp and covered with a lead foil for its cooling effect
1824	Delmond devised a fine, hooked instrument for pulp extirpation
1836	Shearjashub Spooner advised pulp devitalization by Arsenic
1838	Edwin Maynard filed an instrument into a four sided broach
1839	World's first dental journal was introduced
1847	Edwin Truman introduced gutta-percha as a filling material
1850	Hill introduced Guttapercha mixed with lime, quartz and feldspar marketed under the name of Hill's stopping
1850	WW Codman confirmed that the aim of pulp capping proposed by Koecker in 1821, was to form a dentin bridge
1853	Robert Arthur introduced barbs and handles on broaches
1864	Stanford C. Barnum introduced rubber dam
1866	Chase introduced pulp mummification
1867	GA Bowman introduced gutta-percha points for root canal filling
1867	Magitot suggested use of electric current to determine vitality of pulp
1879	Witzel introduced phenol
1880	Brophy used heat to check the status of pulp, traced sinus tract
1883	Perry used gutta-percha wrapped around a gold wire
1883	WE Harding differentiated between pulp capping of an accidental and intentional exposure
1884	Carl Koller firstly used topical local anaesthesia with cocaine
1885	Lepkoski advised use of formalin despite of arsenic to 'dry' pulp

Teble 1.1	Figure of Engladoptics (Contd.)
Table 1.1	Evolution of Endodontics (Contd)
1990	Carlsen and Alexandersen described Radix entomolaris
1993	Torabinejad developed mineral trioxide aggregate (MTA)
1993	Lussi, Nussbacher Grosrey described non-instrumentation technique
1993	APIT/Endex (third gen Electronic apex locator) developed by Frank and Torabinejad
1994	Ben Johnson introduced Profile instruments
1995	McSpadden introduced Quantec instruments
1996	Buchanan introduced Hand Greater taper files
1996	Hoshino and Colleagues introduced Triple antibiotic paste
1999	Endox system was introduced by Haffner and colleagues
1999	Bingo 1020 (fourth generation apex locator)
2000	Edward Lynch and Aylin Bayson developed Healozone
2000	Arias introduced electrochemically activated water as irrigation solution
2001	Clifford Ruddle and team developed protaper system in co-operation with Dentsply
2001	Micro-mega developed Hero Shapers
2002	John McSpadden introduced K3 Endo
2003	Jai and Albert introduced Resilon as an obturating material
2003	Torabinejad introduced irrigant MTAD (4.25% citric acid, 3% doxycycline, 0.5% Tween 80)
2004	Dr Goodis introduced V-taper
2005	Zehnder introduced irrigant HEBP (7% 1-Hydroxyethylidene-1,1-bisphosphonate)
2005	Liberator was introduced by Miltex
2006	Protaper Universal system was introduced
2006	Fukumoto introduced intracanal aspiration technique
2006	Koch and Brave introduced Activ GP
2007	Franklin introduced Monobloc concept
2007	Endovac was introduced by Hoafs and D Edson
2007	Tulsa dental specialities introduced M wire technology
2007	Greater taper series X was introduced by Dr S Buchnan
2008	Dr Richard Mounce introduced Twisted file
2008	Ghassan Yared introduced a concept of canal preparation using only one NiTi rotary instruments
2009	Pierre Machtou, Bob Sharp and Cliff Ruddle introduced endoactivator irrigation system
2009	George Eliades introduced vibringe irrigation system
2009	Endosequence post preparation technique was developed by Dr Ali Nasseh
2010	Redent Nova introduced self adjusting file
2010	Ghasson Yared introduced Reciproc
2011	Dentsply introduced Wave One
2012	FKG Dentaire introduced RaCe
2012	Coltene-Whaledent introduced Hyflex-CM
2012	Micro-Mega introduced Revo-S file
2013	Micro-Mega introduced One shape
2013	Dentsply introduced ProTaper Next
2014	Neolix France introduced NeoNiTi file system
2015	Coltene-Whaledent introduced Canal Pro Cr-2 Endomotor with reverse motion
2015	File retrieval kit by Dr Yoshi Teruachi
2016	Autosyringe introduced by vista dental
2017	Carl Zeiss introduced Civil Zeiss extara 300

OUTCOME OF ENDODONTIC THERAPY

In biology, the term 'outcome' can never be defined. Age old phrase 'body tissues never follow text' is true in all therapies; equally true in endodontics. The 'outcome' is based on several factors, and taking care of each of these factors can minimize failures; however, one factor 'iatrogenic' is beyond the control of all of us. Therefore, the prognosis (the forecast of a disease) may not be definite.

In endodontic therapy, the term 'prognosis' applies to chances of healing; thereby, saving the tooth. The outcome of the treatment is evaluated in terms of clinical normalcy (absence of symptoms) and radiographic normalcy (reduction or disappearance of radiolucency) associated with the tooth. These results are better stated and communicated in terms of healing as follows:

Healed: Follow-up reveals a combined clinical and radiographic normalcy.

Healing: Considering the fact that healing takes considerable time, it is described as a combination of clinical normalcy and reduced radiolucency.

Functional: Follow-up reveals a residual radiolucency combined with clinical normalcy. The residual radiolucency may have been either reduced or remain unchanged in size.

The terms 'healed', 'healing' and 'functional' indicate the outcome of endodontic therapy; routinely used for treatment success.

Factors of Prognosis

There are various preoperative, intraoperative and postoperative factors which influence the outcome of endodontic therapy.

Preoperative Factors

- a. Tooth location: It has been observed that certain teeth (maxillary canines, maxillary second premolars and mandibular canines) have a better prognosis than other teeth; however, any difference between anterior and posterior teeth has not been documented. Maximum failure rate has been observed in mandibular first premolar.
- b. *Symptoms*: Preoperative symptoms may be a reflection of the types and numbers of microorganisms in root canal system. Nevertheless, the healing rate is comparable for both symptomatic and asymptomatic teeth.
- c. *Size of the lesion:* Smaller lesions up to 5.0 mm diameter have shown better prognosis than the larger lesions.

- d. *Periodontal condition:* The preoperative periodontal condition of the tooth does not influence prognosis of the endodontic therapy. Periodontal diseases may advance on its own rate, subsequently tooth loss becomes imminent.
- e. *Systemic health:* The influence of systemic health has not been established to a great extent; however, it is seen that medically compromised patients are at high risk of developing infections.

Intraoperative Factors

- a. *Apical extent of treatment:* Extrusion of filling materials beyond the root end generally results in a poor prognosis. The impaired prognosis may result due to over instrumentation and displacement of infected debris into the periapical area.
- b. Apical enlargement: It has been stated that a larger apical preparation is associated with poor prognosis. Being technique sensitive, extensive apical enlargement is frequently associated with canal transportation, jeopardising canal disinfection. But considering the importance of removing infected root dentin (harbouring intracanal micro-organism), an extensive apical preparation is believed to enhance the disinfection, and favour improved prognosis. Thus, apical enlargement, being technique sensitive, require considerable skill to achieve better results.
- c. *Culturing*: A negative culture obtained before root filling may present better prognosis; however, the technique is not followed in routine.
- d. *Treatment sessions:* The teeth treated in two sessions or less have a better chance of healing than teeth treated in multiple sessions. It is established that teeth treated at multiple visits are at a greater risk of becoming infected with *E. faecalis* and developing persistent apical periodontitis. Also, single visit root canal treatment presents with a similar healing rate as multiple visit treatment and patients experience less frequency of postobturation pain.
- e. Materials and technique:
 - Intracanal medicament: Teeth treated with calcium hydroxide heal better than teeth not medicated at all or medicated with other material.
 - Instrumentation technique: Standardized technique gives better results than serial instrumentation technique.
- f. Microbial elimination: Abundant use of sodium hypochlorite, extensive apical enlargements and dressings with an effective intracanal medicament such as calcium hydroxide provide maximal microbial elimination. As micro-organisms are the primary cause of persistent apical periodontitis; microbial elimination significantly affects prognosis.

Postoperative Factors

Restoration: A well restored tooth that seals coronal cavity effectively and prevents microbial ingress, favours a better prognosis.

FUTURE OF ENDODONTICS

Endodontics is constantly evolving through improvements in our understanding of the nuances of pulp physiology and pathology, coupled with advances in materials and other technological innovations. The future of endodontics lies in exploring the different aspects of the principles of endodontics, facing the challenges and taking the advantage of advancements in research and technology.

The important features are as follows.

Endodontic Imaging

The advent of digital capture systems in the last couple of years have revolutionized the endodontic diagnosis and treatment

The advantages of digital imaging include significant dose reduction, relatively faster image acquisition, ability to enhance images, elimination of wet processing, easier transmission, and archival of images. The digital sensors are slightly smaller than film but sufficient for endodontic purposes.

The future of endodontic imaging relies on wireless sensors, including the newly introduced CMOS-APS sensors (in endodontics, instantaneous images are required, which is best served by CMOS sensors).

The advent of cone beam computed tomography (CBCT) has resulted in widespread adoption of this technology for capturing three-dimensional image. CBCT is useful in diagnosing dental anomalies/developmental disturbances, anatomic variations, calcified canals, broken instruments, vertical root fractures, resorption (external and internal) etc. and especially useful in implant placement.

Endodontic Visualization

The use of optical magnification instruments enables the endodontist to magnify a specified field, which is usually difficult to perceive by the naked eye. The recently introduced Endodontic Visualization System (EVS) incorporates both endoscopy and orascopy into one unit. The improved EVS II System combines the fiber optic orascope and a rigid endoscope. EVS provides optimal magnification for visualization during endodontic procedures.

A variety of additional upgrades for microscope functions have been introduced. Instead of fixed focal distances that limit the microscope to a certain distance, focal distance adapters are available, allowing for easier adjustments during root canal procedures. Extendable (foldable) binoculars were introduced for better ergonomics. Magnetic arrest functions (clutch) are also available for increased stability with use of microscope. LED lights (emission spectrum, 450–550 nm) offer a significantly longer lifetime; however, brightness is compromised as compared to xenon light.

Root Canal Preparation

The concept of pericervical dentin (PCD) (defined as the dentin near the alveolar crest; roughly 4.0 mm coronal to the crestal bone and 4.0 mm apical to crestal bone), is a critical structure and is crucial during transferring load from the occlusal table to the root. The modification in the traditional straight line access helps to preserve the pericervical dentin. With the modern endodontic molar access, the coronal third of the crown can be flared to gain access to the canal orifices instead of the straight line access. The Endoguide Burs (SS White) revolutionized the traditional access preparation allowing shift from conservation to preservation. Preserving the dentin thickness, right from the access preparation to the root canal instrumentation is considered mandatory for long-term success of treatment.

Various rotary systems like Self-Adjusting File System, V-Taper, Safe Siders, Hyflex Files, NeoNiTi, Protaper Next, Single File Systems (WaveOne, One Shape, Komet F360) have changed the sequence in endodontic instrumentation. Wizard Navigator is a newer file system, which the manufacturer claims to face the endodontic canal challenges. Technologies and file design like the M-wire technology, controlled shape memory, hollow tube designs have great and direct impact on the chemico-mechanical debridement. New devices are being designed in apex locator along with the torque controlled gear reduction handpieces.

Root Canal Disinfection

The delivery of irrigant (irrigation dynamics) within root canal system is crucial to achieve the requisite success in treatment. The mechanism by which fluid dynamics can be improved and also the development of newer-effective antimicrobials are under constant research.

The improved delivery systems are Monoject endodontic needles, ProRinse probes, Micromega 1500, CaviEndo systems, the Max-I-Probe, The Endo-Eze system, etc. New irrigation technology will allow clinicians to conveniently choose, dispense, and more effectively irrigate root canal systems.

The use of ultrasonics along with dental operating microscopes is termed as Microsonics. The use of ultrasonic instruments has revolutionized the art of endodontic retreatment.

A new paradigm shift is the Gentle Wave system which utilizes multisonic ultracleaning technology that can quickly, easily and safely loosen and remove pulp tissue along with debris within few minutes. With introduction of lasers to the field of dentistry, various treatment modalities changed. New laser tips have been designed for endodontic disinfection namely PIPS and X-PULSE. Newer technologies are being studied for better treatment modalities in future.

Apart from biocompatible disinfection, many other frontiers in regenerative endodontic research are being currently investigated. These involve tissue engineering strategies that include the evaluation of suitable scaffolds, growth factors, and harvested stem cells to be used in pulpal regeneration. The use of platelet-rich plasma, platelet fibrin, and a gelatin hydrogel as scaffolds are routinely used in clinics. A recent trial involves harvesting stem cells from a donor site followed by *ex-vivo* expansion, sorting, and autotransplantation into a recipient tooth to promote the regeneration of the once lost functional pulp-dentin complex. A bright future is in store for the regenerative endodontics.

Nanotechnology

Advancement in the field of nanotechnology in the past has changed the mindset of clinicians opting endodontics as their field of specialization.

Tiny machines, known as nanoassemblers, could be controlled by computer to perform specialized jobs. Nanorobots could also be the part of endodontic kitty. Replacement of the whole tooth, including the cellular and mineral components, is referred to as complete dentition replacement. This therapy is possible through a combination of nanotechnology, genetic engineering, and tissue engineering. Use of nanosponges introduced in blood stream could reduce toxicity; this could be applied in dental pulp revitalization.

A lot has already been achieved in terms of technological advancements in materials, equipment and still a lot has to be achieved in the field of regeneration and improving biocompatibility of materials. Endodontics would always be in demand in future because the preservation of the natural tooth is the best treatment for the patient, which is the principle of endodontic treatment. With so much of research and advancement carried out in this field, one can proudly say that future of endodontics is indeed vivid and exciting.

BIBLIOGRAPHY

- 1. Blicher B, Baker D and Lin J. Endosseous implants versus non-surgical root canal therapy: a systematic review of the literature. Gen. Dent.: 2008; 56:576–82, 591–592.
- 2. Friedman S. Prognosis of initial endodontic therapy. Endodontic Topic: 2002; 2, 59–58.
- 3. Friedman S. Considerations and concepts of case selection in the management of post-treatment endodontic disease (treatment failure). Endodontic Topics: 2002; 1, 54–78.
- 4. Friedman S and Mor C. The success of endodontic therapy: healing and functionality. J. Calif. Dent. Assoc.: 2004; 32:493–503.
- 5. Goldman M, Pearson AH, Darzenta N. Endodontic success-Who's reading the radiograph? O. Surg O. Med O. Pathol,: 1972, 33; 432–437.
- 6. Heffernan M, Martin W and Morton D. Prognosis of endodontically treated teeth? Quint. Int.: 2003; 7:558–561.
- 7. Hamedy R, Shakiba B, Fayazi S, Pak j G and White SN. Patient-centered endodontic outcomes. A narrative review. Iran Endod J.: 2013; 8, 197–204.
- 8. Kanaparthy R and Kanaparthy A. The changing face of dentistry: nanotechnology. Int. J. Nanomed.: 2011; 6, 2799–2804.
- 9. Lenherr P, Allgayer N, Weiger R, Filippi A, Attin T and Krastl G. Tooth discoloration induced by endodontic materials: a laboratory study. Int. Endod. J.: 2012; 45: 942–949.
- Li X, Kolltveit KM, Tronstad L and Olsen I. Systemic diseases caused by oral infection. Clin. Microbiol. Rev.: 2000; 13:547– 558.
- 11. Miran S, Mitisiadis TA and Pagella P. Innovative dental stem cell-based research approaches: The future of dentistry. Stem Cells Int.:2016; Article. ID7231038: 1–7.
- 12. Murray CA and Saunders WP. Root canal treatment and general health: a review of the literature. Int. Endod. J.: 2000; 33:1–18.
- 13. Ng YL, Mann V, Rabbarran S, Lewsey J and Gulabivala K. Outcome of primary root canal treatment: Systematic review of the literature part 2 influence of clinical factors. Int. Endod. J.:2008; 41:6–31.
- 14. Ng YL, Mann V and Gulabivala K. Outcome of secondary root canal treatment: A systematic review of the literature. Int. Endod. J.: 2008; 41:1026–46.
- 15. Oshima M and Tsuji T. Functional tooth regenerative therapy: tooth tissue regeneration and whole-tooth replacement. Odontology: 2014; 102:123–136.
- 16. Pallasch TJ and Wahl MJ. Focal infection: new age or ancient history? Endod. Topics: 2003; 4:32–45.
- 17. Siqueira JF. Aetiology of root canal treatment failure: why well treated teeth can fail. Int Endod J.: 2001, 34, 1–10.
- 18. Sjogren U, Hagglund B, Sundqvist G, Wing K. Factors affecting the long term results of endodontic treatment. J Endod,:1990, 16; 498–504.
- 19. Smith DE, Zarb GA. Criteria for success of osseointegrated endosseous implants. J Prosth. Dent.: 1989, 62; 567–572.
- 20. Smith AJ, Duncan HE, Diogenes A, Simon S and Cooper PR. Exploiting the bioactive properties of the dentin-pulp complex in regenerative endodontics. J. Endod.: 2016; 42:47–56.
- 21. Trope M. Implant or root canal therapy—an endodontist's view. J. Esthet. Restor. Dent.: 2005; 17:139–140.