The role of immunologic response as a cause of endodontic pain and failure of endodontic treatment, a review

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Abstract

Pain is the most common symptom of a diseased pulp and majority of patients attending the dental clinic normally present with pain. Its management in most cases has been extractions but due to the available and advanced treatment facilities, root canal treatment (endodontic treatment) has become an alternative treatment option. Root canal treatment eliminates root canal flora by chemo-mechanical debridement followed by obturation of the canal.

Following endodontic treatment, patients may still present to the clinic with pain that may be related to a flare-up or Endodontic failure. Undoubtedly the pain may be due to a number of aspects related to local tissue changes, namely, microbial factors, immunological phenomena and other entities. This review aims at assisting the dentist in understanding the role of the immunological response as a cause of endodontic pain and possible reasons for failure of endodontic treatment. Various preventive and treatment options have been outlined in respect to the immunological response.

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Introduction

The dental pulp, like any other connective tissue can undergo changes that may be inflammatory or degenerative. These responses produce a variety of signs and symptoms that clinicians call "pulpal diseases". Even though the pulp often shows remarkable capacity for recovery, painful symptoms and pulp tissue breakdown may follow insults such as caries, dental trauma, or operative dental procedures (1). Clinically, the first signs of dental pulp inflammation are hyperemia, followed by painful symptomatic pulpitis or necrosis of the dental pulp. Following secondary exposure it is only a matter of time before pathogenic bacteria descend into the pulp canal to cause an abscess either within the canal itself or periapically by extension of the infection (2). Though the most common symptom of a diseased pulp is pain, sometimes pulpal necrosis progresses without the patient experiencing pain (3) resulting in some pulp pathologies remaining undetected in vivo (4). This unpredictable response of the dental pulp to clinical insults is frequently encountered in the daily practice of dentistry (1).

Bacterial species are known to play an important role in the pathogenesis of microbial-induced pulpal/periapical inflammation (5). To counteract microbial or "foreign body" invasion, the host defense mechanism is activated. Macrophages thus produced have a greater ability to phagocytose and kill ingested microorganisms or "foreign bodies". Following inflammation, macrophages and lymphocytes play essential roles in cell-mediated mechanisms. During the development of specific immunity, macrophages are required to process and present antigen to immunocompetent T cells. They also serve as "accessory" cells to lymphocytes by releasing soluble factors involved in host defense. Activated T cells serve as key effector cells that are capable of producing lymphokines which modify the behavior of other cells. In this way, they are able to facilitate or suppress an immune response (6). The dental pulp contains the necessary cellular constituents to mount an immunologic defense reaction (7) and although pulpal cells are not able to identify antigens specifically, they provide necessary signals to activate T-lymphocytes which in turn will orchestrate other immunocompetent cells to mount the local immune defense of the dental pulp. Defense reactions of the dentine/pulp complex involve a variety of biological systems, in which the immune system plays a pivotal role (8).

Root canal treatment eliminates root canal flora by chemo-mechanical debridement followed by obturation of the canal to achieve a seal (9). It is generally accepted that the outcome of root canal treatment is to provide a hermetic seal against bacterial ingress into the periapical area (10,11) and studies have shown that success rates of root canal therapy generally approach 90 percent (12). However following endodontic intervention, inter-appointment flare-up or failures may result

and are characterized by the development of pain, swelling or both (13,14). Tissue injury induced by intra-canal procedures and substances extruded through the apical foramen may influence the development of post-operative pain as well as the outcome of root canal treatment (15).

Causative factors of flare-ups encompass mechanical, chemical and/or microbial injury to the pulp or periradicular tissues (16) which may arise due to inadequate control of infection, poor design of the access cavity, inadequate instrumentation and obturation, missed canals and coronal leakage (17). Of these factors, microorganisms are arguably the major causative agents of flare-ups or failures (16).

Following the inability to eliminate the root canal infection, mobilization and further concentration of defense components at the periradicular tissues impede spreading of infection, and a balance between microbial aggression and host defenses is commonly achieved (16). Hence the presence of persistent periapical radiolucency has often been used as a criterion of endodontic "failure" and as an indication for endodontic retreatment (18).

In a flare-up or Endodontic failure, undoubtedly a number of aspects related to local tissue changes are involved, namely, microbial factors, immunological phenomena and other entities. The aim of this review is to emphasize the role of the immunologic response as a cause of endodontic pain and failure of endodontic treatment and to outline various preventive and treatment options.

Immunologic Mechanisms/Components

The immune system is an organization of cells and molecules with specialized roles in defending against infection. There are two fundamentally different types of responses to invading microbes; innate or acquired response. The Innate (natural or humoral) responses occur to the same extent regardless of how many times the infectious agent is encountered, whereas acquired (adaptive or cell-mediated) responses improve on repeated exposure to a given infection. The immune response thus is a biologic phenomenon for protection of an organism, a mediator of injury and under some circumstances a requirement for repair (19).

For the immune response to function it requires antigens. Antigens that elicit immune responses are termed immunogens. Not all antigens are naturally immunogenic. Antigens or immunogens are substances that are regarded as "foreign" to the host and able to stimulate an immune response. Besides bacteria, noxious substances such as degraded protein components, cholesterol, carbohydrates, lipids, nucleic acids or simple chemicals called haptens (19,20) could also act as antigens and elicit a immune response (21). The haptens must be coupled to larger immunogenic molecules, termed carriers, to stimulate a response (22). Even large protein antigens can be made more immunogenic by combining them with an adjuvant — a substance that nonspecifically enhances antigen-specific immunity. Many microorganisms inherently possess adjuvant activity (23). Haptens by themselves are not antigenic, however they may interact in vivo with a host protein (carrier) to form a complete antigen (Hapten + Carrier = Antigen).

Any of the following substances that are used in root canal treatment can act as haptens (19,20).

- various cement base materials (e.g. Zinc oxide eugenol)
- restorative materials (e.g. Silicate, acrylics and resins)
- medicament components (e.g. paraformaldehyde, formocresol, camphorated monoparachlorophenol, thymol, iodine, creosote, creresatin)
- irrigants (e.g. Sodium hypochlorite, hydrogen peroxide, Zephiran chloride, urea, various local anaesthetics)
- root canal cement components (e.g. Rosin, balsam of Peru, zinc, silver, barium, bismuth, formaldehyde, mercury compounds)
- corrosion products (e.g. Silver sulphides)
- even gutta-percha may be a hapten on its own or when contaminated with tissue irritating substances that can initiate a foreign body reaction (24).

It is the interaction of the antigen with the host that results in antibody formation. Antibodies are a group of glycoproteins composed of polypeptides and carbohydrates and five classes of antibodies have been found in human beings (IgG, IgM, IgA, IgD and IgE) (20). Human dental pulps were assayed for the presence of immunoglobulins (25) and analysis showed that IgG was the predominant class of immunoglobulin present, followed by IgA (26).

Though some studies reported no evidence of the biosynthesis of IgM in dental pulps, their presence has been identified in smaller quantities to other immunoglobulins (27). Controversy also exists in regard to the presence of mast cells in the dental pulp and studies have indicated that mast cells are present in noninflamed as well as inflamed pulps (28). Lymphocytes have also been identified throughout periapical inflammatory lesions (29).

Cytokines constitute another group of soluble mediators of the immune mechanism. They act as messengers both within the immune system and between the immune system and other systems of the body, forming an integrated network that is highly involved in the regulation of immune responses (30). Also complement (a complex system) that is produced during immunologic responses, primarily with IgM, helps to promote phagocytosis and lysis of microbes (31). Due to mast cells being found in close proximity to lymphocytes, it is suggested that a functional relationship exists between these two cell populations that may facilitate elicitation of an immune response contributory to the pathogenesis of periapical lesions (32).

Classification of Immunological responses

A widely used classification is that proposed by Gell and Coombs (1975) (33). They classify immunological responses into four main types. Types I, II, and III are immediate reactions based on humoral immunity, and type IV is a delayed reaction based on cell-mediated immunity.

Type I – Anaphylactic Reaction

The type I immunological reaction deals exclusively with reactions of one class of immunoglobulins, IgE (34). It is constantly formed; and has a half life of 2-4 days; in blood. IgE has a special capacity to attach itself to receptors on mast cells and basophils. The mast cells and basophils for which IgE antibody has a marked affinity play a key role in anaphylactic reactions. Ishizaka and coworker (35), showed that the antigen can bridge two molecules of IgE antibody on the mast cell surface. The effect of this reaction is the sudden liberation of stored mediators of inflammation (36) such as histamine, leukotrienes and prostaglandins, which cause the observed allergic reactions. The primary role of these chemicals released from the mast cells appears to be defense against injury; however pathological changes such as bone resorption may occur as well (37). An example of an endodontic material that can cause an anaphylactic reaction is formaldehyde in a root canal sealant (38).

Type II – Cytotoxic Reaction

Type II reactions are mediated by IgG or IgM antibodies and complement. The antibodies are directed toward foreign cells or host cells. Complement fixation may result in cell lysis. Macrophages and other cells may also damage the antibody-coated cells (39). Antibodies binding to cells may not activate complement, but may instead either mask an antigenic determinant or alter cell receptor function. If a cell bound antigen is masked by an antibody that does not permit either complement-binding antibody or an activated cytotoxic T-lymphocyte to react with that cell it is termed a blocking antibody (40). Historically, pulp-necrotizing agents like arsenic trioxide were commonly used in endodontic treatments. They act quickly and devitalize the pulp within a few days. If such an agent diffuses out of the cavity, it can readily cause widespread cell death of gingiva and bone (41).

Type III – Antigen-Antibody Complex Reaction

Immune complex (antibody-antigen) diseases occur when IgG antibodies and soluble antigen form small complexes that lodge in the basement membranes of blood vessels. Subsequent complement fixation results in inflammation (42). When these complexes form, they activate complement. Anaphylatoxins and chemotactic factors are generated which cause an influx of fluid and leukocytes into the area of immune complex formation. The platelets are damaged by the complement activation on their surfaces and they release additional vasoactive amines (43). With the influx of fluid and cells more substrates are available for the reaction causing more complement to be fixed and more cells tend to invade the area of inflammation. The polymorphonuclear leukocytes attempt to ingest the immune complexes, but cannot surround the endothelial cells that are binding the immune complexes and consequently discharge their lysosomal granules against the endothelial cells (37). This causes damage to the endothelial cells and the surrounding tissue and intensifies the inflammatory reaction. The intensified inflammatory reaction imitates the coagulation pathways and fibrin is deposited locally. If the

lesion is due to a single dose of antigen, the inflammation resolves and the tissue damage is repaired with residual scarring. If the antigen deposition is continued however, chronic inflammation occurs with more severe tissue damage (42). Foreign materials trapped in periapical tissues during and after endodontic treatment can perpetuate a host defense response (43). Host defenses results in local inflammation, resorption of hard tissues, destruction of other periapical tissues, and eventual formation of various histopathological categories of apical periodontitis, commonly referred to as periapical lesions.

Type IV - Delayed Hypersensitivity Reactions
Cell mediated immunity, or type IV immunological reaction does not involve antibody (44) but stimulates lymphocyte cell proliferation. This type of hypersensitive (allegic) reaction occurs when an antigen interacts with antigen-specific lymphocyte that release inflammatory and toxic substances, which attract other white blood cells and results in tissue injury. The reaction between antigen and T cell is facilitated by the presence of reactive sites on the surface of the lymphocyte. These sites have many features in common with the combining sites of immunoglobulin molecules. Delayed hypersensitivity reaction is initiated by interaction between previously sensitized lymphocytes and antigenic materials. Human periapical lesions develop as a result of a pathological immune response to continuous stimuli from infected root canals and it has been suggested that T cells may play an important role in the development of periapical lesions (45).

Immunologic concepts related to pulpal and periapical pathogenesis
The complement system plays an essential role in host defense against infectious agents and in the inflammatory processThe complement system can be activated by two different pathways: the classical (antibody-dependent) or alternative (antibody-independent) complement pathway. The classical pathway is activated by the binding of antibody molecules to a "foreign particle" while the alternative pathway is activated by invading micro-organisms and does not require antibody. This pathway plays a major role in host defense against bacterial infection. While these two roles appear distinct, they are linked. Both the natural antibody and classical pathway complement work together in host protection against bacterial infection on the one hand but, on the other, they co-operate to induce inflammation (46).

With the development of caries, bacteria and their products can induce an acute inflammatory response within the pulp and if a carious lesion is allowed to progress, macrophages, lymphocytes and plasma cells (mediators of the immune system) become evident (47). Due to the restricted room for expansion available within the pulp chamber, the inflammation spreads to the periapical tissues via the root canal and is characterized by a chronic inflammatory cell infiltrate (48,49). All bacteria that normally inhabit the oral cavity theoretically have the capacity to invade the root canal space during and following pulp necrosis and to participate in the infection of the canal and ultimately, to enter the periapical tissues (6,50).

Besides the various dental manipulative and restorative procedures (4), pulpal necrosis mediated by bacterial contamination can also lead to the accumulation of many inflammatory products within the root canal system (47) resulting in pulpal destruction and ultimately eliciting a host defense reaction in periapical lesions (21,45). Other primary and independent co-factors of necrotic pulp tissue or root canal fillings can also elicit a host immune response (24,51,52). The invasion of host tissue by microbes or their products frequently induces a wide variety of immunopathologic reactions (53). The immune response taking place at the periapical region is predominantly cellular (54) although periapical tissues have components that are necessary for the cellular and humoral immune response (29). The periapical lesions often contains an intense infiltration of plasma cells, lymphocytes, macrophages and scattered Russell's bodies, long accepted as the cardinal histopathological features of cellular immunological activity (55). The presence of immunocompetent cells has been demonstrated in human periapical lesions suggesting that the immune response in such sites is quite active (45). It has been suggested that macrophages have a central protective role in both innate and adaptive immunity and antigen-specific immune response. Their activation may occur by cytokines produced by antigen-activated T-lymphocytes; by bacterial endotoxin, as part of the innate immunity; or by both these processes (56).

Polymorphonuclear cells and mononuclear phagocytes are key components of the host defense against invading microbes (29). Polymorphonuclear cells tend to predominate in acute inflammation, whereas mononuclear infiltrate is more often seen in chronic inflammation. The nature of leukocyte infiltrate affects the progress of the disease (53). Polymorphonuclear cells and macrophages migrate to the periapical lesions and phagocytose pathogens as a first line of defence. Dead polymorphonuclear cells are quickly phagocytosed by macrophages and this disposal system plays a role in maintaining chronicity of the lesions (21). Inflammatory immune responses are initiated either in the pulpal tissue or periapical area when antigens are introduced into the root canal. Microbial antigens could also be slowly released from disintegrating macrophages. Repeated release of antigen could stimulate the formation of B and T lymphocytes both locally and in the surrounding lymph nodes. T- and B-lymphocytes are programmed to respond to specific antigens (29). Specific antibodies and/or sensitized T-lymphocytes could then react with any of the various antigens and the periapical response that forms could be one or a combination of protective or allergic reactions. The repeated slow release of microbial antigens from the periapex could first sensitize host cells at a secondary site, and then later cause an immunologic response against the host's own cells or products. This microbial incited auto-immunity could be considered as a form of focal infection as the periapical area is surrounded by a dense wall of alveolar bone. The cells and products of the periapical granuloma would be localized, allowing for prolonged retention of antigens at this site. Depending on the nature and quantity of the antigens, as well as the duration of exposure of the periapical tissues, a variety of tissue changes can occur including bone destruction in the periradicular tissues (21,40).

Countless molecular and cellular inflammatory responses lead to development of resistance to reinfection. This acquired immunity reflects the immune system's ability to recognize and adapt to specific foreign molecules (57).

Elderly patients experience a marked decline in cell-mediated immune function and reduced humoral immune function and age-dependent defects in T and B cell function are readily demonstrable in elderly patients (58).

Endodontic pain

Pain is the most common symptom that compels patients to seek medical and dental therapy and constitutes a serious health and economic problem (59). Pain is usually indicative of a reaction to tissue damage and to some extent usually connotes the extent of the damage (4). Due to the anticipation of pain, many patients fear endodontic procedures although pain experienced during endodontic treatment is often less than anticipated. Younger people anticipate and experience higher pain levels and women are more likely than men to anticipate pain, but not necessarily experience, higher pain levels (60). Although pain is well managed in many endodontic patients, there may be a group of patients who do experience pain due to inadequate administration of local anesthesia (61).

Pain is the only sensation that is normally evoked by stimulation of the dental pulp and this is because the sensory innervations of the dental pulp consists of A-delta and C-fibre types. Pain is provoked when variety of substances are released or injected into the tissue as a result of trauma, infection, allergenic reactions, neurogenic reflexes or central emotional changes from cell membranes, mast cells and nerve endings. Quality of pain depends not only on the stimulus but also on the pattern of innervation of the tissues to which it is applied (59). Subjects who experience pulsating dull lingering pain (clinically diagnosed as pulpitis) showed a poor correlation between magnitude estimates of their mixed pain percepts and the total flux of A-delta nerve activity. Bradykinin and histamine evoke dull pain in the majority of cases by excitation of the pulpal C fibres (62). When there is tissue injury, many cells are destroyed and the intracellular material is dumped into the surrounding tissues, such that the normally innocuous substances build up to a level in which they become transmitters for the activation of pain receptors and inflammation. As pain receptors are activated the same local chemical mediators are recruiting cells to initiate the inflammatory process in the area of injury. As the biochemical mediators build up in the injured tissues more and more pain impulses reach the central nervous system (63). In response to irritants, inflammatory mediators are non-specifically released and the pain threshold of sensory nerve fibres is lowered (64). One of the perplexing questions in endodontics has been the absence of symptoms in some patients with

gross caries, pulp pathologies, periapical lesions or failing root canal treatments. This lack of symptoms despite tissue injury may be the result of neuroinhibition. Excitatory input thus principally serves as a modulating role. Therefore, inhibitory pulpal nerve mechanism could occur until such a time as excitatory modulators exceed threshold levels and elicit a pain response. This paradigm supports the general observation that pain is an infrequent or late sequelae to caries or pulp and periapical pathology (65). A relationship between specific microorganisms and the presence of spontaneous or previous pain, tenderness to percussion, pain on palpation and swelling has been suggested (66). Microorganisms can participate in causation of interappointment pain in the following situations: apical extrusion of debris; incomplete instrumentation leading to changes in the endodontic microbiota or in environmental conditions; and secondary intraradicular infections. The causative factors of interappointment pain encompass mechanical, chemical, and/or microbial injury to the pulp or periradicular tissues, which are induced or exacerbated during root canal treatment (67). The factors that influence postoperative pain after root canal treatment are not completely understood but pain is a fairly common side effect. This kind of pain may last for several hours to several days and is dependent upon the damage sustained by the periapical tissue and the nature of the damaging agent (68). While the development of pain is related to the intensity of tissue damage, treatment outcome is more dependent on the persistence of the source of injury. Procedural errors are the main causative agents of either post-operative pain or persistent periradicular lesions. However, even when the treatment has followed the highest standards, post-operative pain can occur and periradicular disease can persist, albeit at a lower incidence when compared to teeth treated to a poor technical standard (15).

Failure of endodontic treatment

Various factors have been reported to contribute to failure of endodontic treatment, mostly notably the presence of intraradicular infection (69,70), foreign materials (71), or presence of infection in the periapical tissues (72). A flare-up following a root canal treatment appointment is a significant problem. The flare-up phenomenon is complex and although not well understood undoubtedly involves a number of aspects related to local tissue changes, microbial factors, immunological phenomenon and other entities (13). Furthermore, microorganisms are very frequently implicated with failures in treatment (73) as routine endodontic procedures may not fully achieve removal of microbes in clinical practice because of the anatomical complexities of many root canals, and limitation in access by therapeutic agents to the microcanal system (74).

Since cementum is impermeable to bacteria, bacteria in the dentinal tubules do not invade the periodontal structures but in cases of root resection bacteria in the dentinal tubules could invade the periapical tissues (75). Organisms may therefore remain in the dentinal tubules, and in the grooves and other irregularities of the canal system. If they remain in sufficient numbers and in an adequately supportive environment, they may multiply and reestablish clinical contamination of the pulp space (76). Sealed root canals can be re-contaminated under several circumstances (77):

- if a patient has had endodontic treatment but has delayed placement of permanent restorations
- if the seal of the temporary filling material has broken down or
- if filling materials and /or tooth structures have fractured or been lost.

When these situations occur, the coronal portion of the root canal system is exposed to oral flora. The question then is how quickly the entire root canal becomes contaminated again and to the point that re-treatment of the canal may be necessary. A major contributing factor to post operative inflammatory response may be endodontic over-instrumentation as the introduced foreign materials and endogeneous substances tend to sustain a reaction (78). If the macrophages and giant cells that accumulate at the site of "foreign body" reaction are not able to degrade the foreign materials, the endogeneous substances sustain the reaction by becoming the major sources of inflammatory and bone resorptive cytokines and other mediators (24).

After instrumentation and obturation of the root canal moderate or severe pain may temporarily be a problem depending on the intensity of the inflammatory process at the periapical region (79). According to Hession (1981), the most common causes of failure after completion of treatment are ineffective three dimensional sealing of the canal system, short fills (untreated canal space), lateral voids, fills with sealers or

medicated pastes only, gross overextension of filling materials or presence of a cyst that fails to heal (80). The management of postoperative pain usually involves occlusal reduction, intra canal medications, administration of systemic analgesics, anti-inflammatory drugs or antibiotics. In some cases of persisting pain, retreatment may be required and in rare occasions, trephination or surgery (81). Two-visit endodontic treatment with intracanal medication was found to be effective in reducing postoperative pain of previously symptomatic teeth and decreased the number of flare-ups in all retreatment cases (82).

Retreatment decision making in everyday clinical practice normally should be based on simple principles, namely in order to achieve the best overall results. Endodontic treatment failures occur in as a result of a number of factors some of which can be controlled by the operator whilst others are unavoidable. The long-term success rate of endodontic treatment has often been thought to be very high (12) although studies reported in the literature do not support this perception (83).

If previous attempts of root canal treatment were not performed with the most sophisticated technique and clinical expertise, teeth regarded to be failures might still have a good prognosis when re-treated using more sophisticated technique and/or clinical expertise. This should be considered prior to extractions as many patients are quite averse to the prospect of loosing a natural tooth and decision to extract should never be taken lightly (84).

Preventive and treatment concepts

The major pathways of pulpal contamination are exposed dentinal tubules, direct pulp exposure, lateral and apical foramina (21). Bacteria or their products are considered to be the primary aetiological agents of pulpal necrosis and periapical lesions and their elimination is one of the most important steps in endodontic therapy (73). Hence the goals of root canal treatment are to disinfect the root canal system and to prevent subsequent re-infection. The disinfection is attempted with endodontic instruments (85), antiseptic irrigation solutions and intracanal medicines (86). Accurate diagnosis, knowledge of the root canal morphology and the principles of modern preparation techniques are all essential so that appropriate chemical cleaning and disinfection of the entire root canal system may be accomplished (87). Careful oral health assessment as a foundation to good treatment planning and quality dentistry is not new, but there are a number of important new perspectives emerging across countries and healthcare systems in terms of the content and role of such an assessment in modern dental practice (88). At the end of endodontic treatment the repair process starts and is characterized by cell proliferation and formation of organic matrix resulting in root apex sealing. The repair process may be interrupted due to various reasons, even the irritant potential of a sealer may retard or prevent repair during this initial phase. Repair process may also be impaired due to variable losses of connective tissue caused by the pathological process itself or due to the aggression of the operative steps preceding the sealing procedure (89). There is a need to emphasize that although there is enormous potential for endodontic success; clinicians are, at times, confronted with post-treatment disease (90). Up to 80% of endodontic patients who report with preoperative pain continue to experience some level of pain following the endodontic procedure. Endodontic pain is often associated with chronic inflammation, the presence of bacterial by-products, influx of primed immune cells and activation of the cytokine network and other inflammatory mediators (91). Various drugs have been used to interfere with inflammation and to prevent or stop endodontic pain. These drugs include nonsteroidal anti-inflammatory agents and steroids and in severe cases of post treatment endodontic pain the use of intracanal non steroidal anti-inflammatory agents has been suggested (92). Other treatment regimens for the relief of pain during endodontic therapy include relief of occlusion, pre-medication, establishment of drainage, and intracanal and systemic medications (93).

Although endodontic procedures and some acute endodontic infections can cause bacteremia, there is no clear evidence that microorganisms from the root canal can cause diseases in remote sites of the body hence prescription of systemic antibiotics in endodontic therapy is rarely necessary. However, there is a risk in some compromised individuals, and prophylactic measures should be taken. The use of antibiotics in endodontics should be highly limited and restricted to a few cases because of the emergence of bacterial resistance against most known antibiotics (94).

It is suggested that in order to achieve the best overall consequence a periapical lesion in a root filled tooth that is not expected to heal should be retreated. Arguments to withhold retreatment should be based on (i) respect for patient autonomy, (ii) retreatment risks or (iii) retreatment costs (18). It is only when non-surgical endodontic therapy has failed to bring about healing that endodontic surgery is indicated and surgical re-treatment is contraindicated when unlikely to improve the prognosis (95).

Recent changes with enhanced abilities and clinical results have made it possible to perform endodontic treatment more efficiently, with improved precision and greater patient acceptance (96). Some of the most keenly debated issues in endodontics have revolved around where to end the root filling, as well as cleaning and shaping and obturation techniques (97). Endodontic treatment is usually considered successful only when the patient exhibits no clinical signs or symptoms and when radiographically there is evidence of complete or at least substantial healing. However many teeth that do not fully meet the criteria for endodontic success may remain asymptomatic and functional for many years (84). Preventive measures against infective flare-ups include adequate selection of instrumentation techniques that extrude lesser amounts of debris apically; completion of the chemo-mechanical procedures in a single visit; use of an antimicrobial intracanal medicament between appointments in the treatment of infected cases; not leaving teeth open for drainage and maintenance of the aseptic chain throughout endodontic treatment (16).

Conclusion

The immune response that causes endodontic pain or failure of endodontic treatment is complex and variable but can be avoided by adherence to the principals of endodontic treatment procedures. This will undoubtedly enhance the quality of the initial treatment and prevent endodontic re-treatment.

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A: Yes, yes, he has been put on complete rest, but he doesn't follow.

B: After all he has to practice for fighting coming elections