Future Research Directions in Pulpal Biology, Endodontic Materials and Endodontic Techniques

Abstract: The rapid evolution of Endodontic as a dental speciality and the increasing demands to identify the biological basis for treatment have resulted in a plethora of research activities designed to address many unanswered questions. However, even with these undertakings, Endodontics has failed to receive the necessary support of investigators and support agencies around the world to pursue basic questions and treatment modalities which have been the subject of empiricism for years. While other dental disciplines garner the majority of available investigative dollars, "What's the big issue about this little tissue?" The purpose of this paper is to provide a brief analysis of research endeavors in the area of pulpal biology, directives for future investigative areas, perspectives on technological advances in endodontic therapy, and incentives and challenges to future pursuits.

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INTRODUCTION

The dental speciality of Endodontics and science of Endodontology, which are concerned with the morphology, physiology and pathology of the human dental pulp and periradicular tissues, have been recognized clinical and biological sciences for many years. Their study and practice encompasses the basic clinical sciences, including biology of the normal pulp; the etiology, diag nosis, prevention and treatment of diseases and injuries of the pulp; and, associated periradicular conditions. Concomitant with the recognition and identification of this focus is the pressing need to pursue, not only the delineation of the biological mechanisms which interplay in selected treatment modalities, but also the development of new treatment parameters which will enhance the delivery of care and the quality of the biological response to such. This paper will address both areas of concern, biological and clinical, providing contemporary and futuristic concerns and directions.

Pulpal Biology

Sixty years ago, Blayney(1,2) succinctly identified the need to pursue something greater than just the "magic cure" or the "novel technique", and to focus on the biological basis of treatment.

"Whenever a pulp is removed and the canal treated and filled in a manner that is compatible with or favorable to a physiologic reaction, we may expect a satisfactory percentage of success. Also, whenever treatment is carried on in such a way as to antagonize biologic processes of repair, we will continue to have many failures. As we see the question, it does not materially matter if an operator uses one style of an instrument, while another prefers a broach of a different pattern, provided each will do the task for which it was designed. The crying need is not a new technic, a new drug or the like, but a better and more keen appreciation of the processes by which nature repairs traumatic injury or overcomes an infectious process.''(1)

"I believe society will be better served if the rank and file of the profession will place pulp-canal therapy on a biologic basis." (2)

It is from this concept that the study of pulpal biology has emerged over the past six decades, and definite strides have been made in th e delineation of the pathophysiological processes in this minute organ.

The very tissue that is produced by the pulp, the dentine, has served as a focus of investigation for many

years. Its uniqueness as a tissue encompasses many aspects including pulpal repair, anatomical configuration, innervation and sensitivity. Because dentine provides a protective barrier to the free diffusion of noxious substances to the pulp, it must be regarded as being in a physiological continuum with the pulp. Likewise, because of its structural dentinal tubular configuration, the dentine can assume a varied role in the diffusion of substances across and along its coursing communications. Pashley(3) has clearly identified, in the animal model, the key challenges that face both the clinician and the scientist in understanding and evaluating the role of dentine in both the health and disease of the dental pulp. However, application to the human model has yet to occur, and therefore extrapolation of findings its cautioned. Within the necessary investigative activities is the role of the smear layer in both endodontics and restorative dentistry, with a focus on microleakage, the role of sclerotic or irritational dentin, the role of peritubular dentin, and, mechanisms responsible for the production of intratubular crystal formation which serve to effectively block tubule permeability. In essence the key to understanding pulpal biology is to understand how external influences gain access to and effect the normal pulpal physiological processes.

The dental pulp is composed of loose connective tissue, blood vessels, nerves, ground substance, fibroblasts, odontoblasts, and mesenchymal cell. As a mature organ, its primary functions are to generate sensory neural activities which give rise to pain sensations in response to irritational' stimuli, and to elaborate preparative dentin as a protective response. The ability of the pulp to perform these functions in a consistent manner is predicated on the integrity of its haemodynamnic processes which provide nutrients and oxygen to the cellular and tissue components and remove the waste products of metabolism. Thus, as indicated by Kim(4), the understanding of pulpal heamodynamics and their regulation is crucial to understanding the character of the pulp as a living and functioning entity. This is especially true as it relates to the understanding of pulpal inflammation due to caries, restorative procedures, vital pulp therapy, trauma and periodontal disease.

Recent scanning electron microscopic structural studies by Takahashi and others (5), have delineated a profound difference in the coronal and apical pulpal vasculature. These findings characterised the nature of the pulpal microvasculature in the odontoblastic layer, the adjacent cell-free and cell-rich zones, and in the center of the pulp, and served as additional support for the studies of Kim(6) on the microcirulation of the dental pulp in disease and health. Further studies (7,8) have correlated this information with various physiological techniques and have shown that there is a close relationship between sensory nerve activity (pain) and the microcirculation of the pulp. This has led to the development of laser Doppler flowmetry which is now being used to assess the status of the pulpa vasculature in diagnostic situations. However, these areas of investigation and application reopen avenues for continued research, as there are many unanswered questions relative to the precise role of the pulpal microvasculature in both a healthy and an aberrant pathophysiological state.

For years the nature of pulpa sensory mechanisms has been open to speculation and debate. Numerous neuroanatomical methods have been used to investigate these proposed mechanisms, with no def inite, clear picture emerging as yet. This is due to many of the shortcomings posed by the various techniques employed, such as tissue preservation, decalification, histological processing and specimen viewing and interpretation. Even with recent advanced techniques of autoradiography(9,10) and immunocytochemistry (11,12), a clear understanding of the types of nerve fibers that innervate teeth, where they terminate, how they interact with pulp cells in normal and pathological states, and how those cellular events relate to dental pain and clinical treatment, is not available.

Byers(13) recently identified a number of key questions relative to the investigation of dental innervation and pain, which are all currently unresolved to varying degrees. These questions focus not only on the paucity of knowledge that is available concerning this issue, but also projected areas of research which should receive attention, if the structure of dental innervation in normal and pathological states is to be understood.

1. What types of nerve fibers innervate teeth and where are their terminals?
2. What happens to dental innervation when teeth are hypersensitive, inflamed, injured, or anesthetised?
3. What neural mechanisms cause dentinal pain and how do they compare with pulpal and periapical pain mechanisms?
4. To what extent do sensory nerve fibers interact with pulp cells?
5. Are there non-nociceptive sensory fibers in teeth? If so, what is their function?
6. Are there sympathetic fibers in dental tissue and to what entent do they affect or interact with sensory fibers?
7. Can pulp pain be diagnosed with more precision and be more clearly distinguished from periodontal pain problems?
8. What central pathways carry dental somatosensory information and how is that information processed in normal animals compared with various dental pathological conditions?

Needless to say, these issues pose a termendous challenge to both the scientist and the clinician. Even less is known about the pathophysiology of the intradental nerves during the carious process and the advancing inflammation in the pulp , as well as the reactions to iatrogenic damage to the dentine and the pulp. However, newer technology which may assist in the delineation of the questions posed is emerging, and consists of the following: recombinant DNA technology for neural delineation, ligand-binding techniques for the determination of specific membrane receptor molecules, cell culture techniques for specific neural cells, increased numbers of antibodies for enchanced immunocytochemistry, voltage sensitive dyes to identify specifically activated neural elements, enchanced axonal transport techniques and the application of sophisticated computer analysis and microscropic techniques(13).

Once the protective barriers of enamel and cementum are altered by restorative procedures, trauma or caries, and the dentine is exposed, the pulp undergoes a wide variety of changes. In recent years there has been a refocus on the effects of bacteria and their products on the dental pulp. When these substances are applied to exposed dentin, inflammatation is produced. However, most studies have focused on responses produced by specific organisms. Unfortunately, this type of investigation does nor represent a true clinical situation, where a large number of varied organisms are involved and each bacterial species may produce a variety of different inflammatory inducing agents both during growth and disintegration. Likewise bacterial sampling and identification also poses problems in the determination of the exact relationship between bacteria and pulpal sequelae. Many of these difficulties focus on microleakage in restorative dentistry and endodontics and the ability to test for the presence of bacteria and to correlate the findings with extent and nature of pulpal and/or periradicular inflammation. This is especially true with the recernt identification of significant anaerobic bacteria and their implication in disease processes of the pulp, periradicular tissues, and reinfection of the root canal system. Regardless of these concerns, it has been established that both restorative materials and root canal filling materials can and do exhibit microleakage -hence the perfect pathway for bacterial ingress. Therefore, not only is the profession of dentistry faced with the improvement of restorative materials, but also the techniques used in their placement. Concomitantly, it is faced with identifying the nature of the bacteria that have the capability of penetrating restorative margins and root canal and root-end filling materials, in addition to their combined pathological mechanisms. Only then can the inflammatory processes initiated by these entities be understood. In this scenario an experimental pulpal and/or root canal model could be designed in which defined bacterial combinations can be studied for specific factors, such as virulence, the interplay of growth factors, toxin production, enzyme elaboration, and toxic metabolic end products. Once developed, this model could serve as a screening mechanism for restorative materials, endodontic materials and techniques to place such. One such model has been developed, albeit in its crudest form, which has identified the nature of leakage and the recoverable presence of specific bacteria which have transgressed the obturated root canal system(14). However more clinically relevant parameters must be integrated into these model systems if data is to be of significance . Findings from these investigations can have a significant impact on treatment modalities because of the greater understanding of the pathophysiological processes which are taking place in the pulp or periradicular tissues, in addition to identifying the short-comings of materials and placement techniques.

Finally, the identification of immunoglobulins in periapical lesions by Naidorf(15) in 1975, the confirmation of immune components in normal and inflamed human dental pulps by Pulver and coworkers(16) in 1977, and the identification of pulpal immunoglobulins to oral microorganisms by Falkler (17) in 1987, have opened the doorway to immunological investigation in pulpal biology and endodontic research. It is because of the unique site of the pulp and associated periradicular tissues that many conventional immunological investigative techniques connot be used to study the changes that occur during injury and inflammation. Likewise, because of the unpredictability of pulpal and periradicular tissue responses to injury, no universally accepted model is available to evaluate a reproducible inflammatory state. However, with the application of radioimmunodiffusion techniques, immunofluorescence techniques, immunoenzymatic techniques, and enzyme-linked immunosorbent assay (ELISA) techniques a greater understanding of the pulpal and periradicular inflammatory process can be achieved which may lead to the development of an in vitro/invivo model for future research.

As can be seen, the biology and pyhsiology of the dental pulp and surrounding tissues, comprise a complex set of variables for which normal and pathological responses remain to be clearly defined. Until these issues can be addressed and identified, it will be very difficult to move forward with significant advances in restorative dentistry and endodontics materials and techniques.

Endodontic Materials

Endodontic materials comprise a multitude of various substances from obturation or filling materials, to sealer/cements, pulp capping materials, root-end filling materials, irrigants, and antimicrobial materials. All materials

used in endodontic procedures must undergo multiple evaluative tests, such as cell culture, implantation, and usage tests(18,19). When using these tests, there are a broad range of characteristics which must be considered, such as toxicity, tissue injury, mutagenicity and carcinogenicity. Guidelines for the use of these tests to assess material properties have been published by the American Dental Assosiation(20) and the Federation Dentaire internationale(21). While the application of *in vitro* test methods can provide a certain amount of material with limited parameters of extrapolation, the use of *in vivo* testing can help to identify the complex interactions betweeen the material and the host tissue. Therefore, the use of a battery of tests designed to give as complete a spectrum of information as possible on a new material is warranted before wholesale distribution and widespread patient use occurs.

Presently, very few new materials have been developed for use in endodontic therapy. However, this may be somewhat fortuitous because there still is a paucity of information available concerning the use of materials which have been used for decades, including calcium hydroxide and zinc oxide-eugenol (ZOE). While these materials have provided varying levels of success when used as capping agents, roots canals sealers, and most recently as a root-end filling material (ZOE), their properties are far short from the ideal when considering the ultimate goal of endodontic therapy as not only being tooth retention, but also complete healing of the pulp and/or periradicular tissues. To take this concept one step further, in order to identify materials for use in endodontic therapy (which includes non surgical and surgical treatment), that will achieve this ultimate goal, the characteristics of these materials must be defined in light of what is known and what is ideal. Therefore, research in this area must be directed to the development of materials which prossess the following properties or characteristics.

1. They must possess antibacterial properties.
2. Rather than just being biocompatible, they must be bioinductive to the formation of new tissue. In the case of the pulp it must be hard tissue; in the periradicular region it must be both a hard and soft tissue response.
3. The materials must adhere to tooth structure (primarily dentine) and be impervious to moisture and microleakage from both the oral environment and the periradicular tissues.
4. The materials must be immune to fluid contamination during placement and set, or they must use and incorporate the available fluids in their setting reaction.
5. A slight expansion upon set would be ideal, however, shrinkage is unacceptable.
6. The materials must not induce any cellular aberration in the host, and ideally should not result in any long term chronic inflammatory response.
7. The materials should not be affected by the presence of a smear layer, as a complete removal of this layer is all but impossible.
8. Dentinal tubules, as well as the apical foramen, accessory and lateral communication, and the coronal orifice of the root canal system must be capable of being hermetically sealed. Therefore, the material must be able to flow into the intricacies of the prepared root canal system and/or condensed into such.
9. Clinical parameters and handling characte ristics of the material must be user friendly.
10. The materials should not be developed as a substitue for thorough removal of tissue debris and bacterial contaminants.

The continued use of antimicrobial agents in the root canal system during treatment should be eliminated, as most often they are used as a panacea for poor root canal debridement. Research should continue in the development of enhanced root canal irrigants, which cannot only debride and dissolve the tissue remnants, but can also dissolve the smear layer and condition the dentine for an adhesive root canal filling material. Efforts should also be directed at pulpal preservation, as endodontic therapy must include as focus on wound healing in the pulp as well as the periradicular tissues. As with previous discussions, the development of in vitro models with in vivo applicability are essential to explore futuristic advances in endodontic materials research.

Endodontic Techniques

As with endodontic materials, very few new or innovative techniques have been developed which have had a major impact on the practice of endodontics. To put them in perspective, a brief listing is indicated.

1. Electronic apex locators - These have somewhat eliminated the need for excessive radiographic exposure, however, they are not foolproof. Likewise, radiographs can provide a wealth of information not available with these devices.
2. Fiber optics - T hese have been a boon to endodontics in both diagnosis and treatment. However, their usefulness has defined parameters and ends therein.
3. Sonic and ultrasonic systems - These instruments have assisted the operator in achieving a greater degree of canal cleanliness, with some ease in preparation in the middle and coronal thirds of the canal. To date however, their use and acceptance is limited, and further research is necessary as well as enhanced

technological improvements before there is a general acceptance of their purported benefits.

4. Obturation systems - There have been, and continues to be, a plethora of obturation devices and techniques on the market. These primarily consist of thermoplasticised gutta-percha systems or applications. To date none have been able to demonstrate the achievement of a hermetic seal in the root canal, with varying degrees of microleakage and adaptability evident. While the concept appears valid, the technology is lacking because of material shortcomings.
5. Radiographic techniques - The most important advancement in this area may be radiovisiography. While exceedingly promising, costs and equipment are burdensome at present.

The biggest area of development which may provide potential important advances for endodontic applications in the future is in the area of lasers. Their use in canal sterilization, preparation, and obturation has been proposed, along with the removal of broken instruments and posts(22)· Likewise, surgical endodontics, including the cutting of soft and hard tissue, root-end resection and sealing has also been identified as uses for the laser, primarily the Nd:YAG system(22).

While a brief overview of contemporary techniques and developments may seem impressive, very little has evolved which has significantly advanced the ascribed goals of endodontics. What is even more alarming is that methods of evaluation for these presumed advanced techniques are crude and do not represent the meaningful gathering of information. For example, dye microleakage tests are used to evaluate a number of clinically advoca ted techniques. Yet these tests are nothing more than stagnant methods to evaluate a dynamic process, and their information is not only limited but subject to significant misinterpretation. Therefore, along with the development of new endodontic technologies must be the concomitant evolution of evaluative techniques, which will provide the researcher and clinician with meaningful data directed at a course of action compatible with technology and material availability. Future directions for endodontic technology shoul consider the following.

1. The development of delivery systems to manage the materials discussed in the previous section.
2. Three-dimensional radiographic imaging techniques that are computer linked and computer assisted for accuracy and precision. Signficant in this area would be the ability to assess the three-dimensional anatomy of the pulpal space prior to and during treatment.
3. The development of diagnostic tools in which a greater accuracy in the status of the pulp can be determined by the clinician. While laser Doppler flowmetry is a step in that direction, the ultimate goal is to be able to establish the true pulpal status in the range of sick ness or health and its ability to heal or not. The concept of vital or nonvital is archaic and obsolete, yet its concept will die hard!
4. Techniques designed to enhance and simplify canal cleaning and shaping are essential, possibly with the use of laser probes in the canal system.

Challenges to the development of new technologies and materials in endodontics are truly overwhelming, and can only be achieved primarily through the dedication and driving interest of those in endodontic academic and research pursuits. However, there is a serious concern that the critical mass of personnel dedicated to these endeavors is dwindling, Therefore, in addition to the need to develop new materials and techniques, there must be a concerted effort to redirect human resources to this focus to ensure the viability of endodontics and endodontology for the future.

Summary

Through the combined efforts of biological and clinical research, advances in pulpal biology can be intergrated with clinical treatment parameters. It is through this integration that the ultimate goals of endodontics and endodontology can be achieved, and the practice of quality dentistry can be attained. To do so however, requires a committed group of professionals, linked for this purpose and dedicated to quality in the pursuit of these goals. As defined by the historian Tuchman, this does nor allow for compromise at any level.

> "Quality means investment of the best skill and effort possible to produce the finest and most admirable result possible. Its presence or absence in some degree characterises every man-made object, service, skilled or unskilled labor-laying bricks, painting a picture, iroining shirts, shoemaking, scholarship, writing a book. You do it well or do it half-well. Materials are sound and durable or they are sleazy; method is painstaking or whatever is easiest. Quality is achieving or reaching for the highest standard as against being satisfied with the sloppy or fraudulent. It is honesty of purpose as against catering to cheap or sensational sentiment. It does not allow compromise with second rate.'

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