

A Practitioner Survey of Opinions Toward Regenerative Endodontics

Ingrid Epelman, DMD, Peter E. Murray, PhD, Franklin Garcia-Godoy, DDS, MS, Sergio Kuttler, DDS, and Kenneth N. Namerow, DDS

Abstract

The success of regenerative endodontic procedures requires practitioner acceptance, but little or no evidence is available. The purpose of this survey was to collect the opinions of attendees of the 2008 Endodontic Board of Diplomates 2008 Summer Conference on the issue of regenerative endodontic procedures (REPs). After Nova Southeastern University institutional review board approval, 100 copies of a survey were circulated, and 56 completed surveys were returned anonymously. The survey found that 96% of participants thought that more regenerative therapies should be incorporated into treatments. Although only 14% of participants had used umbilical cord or stem cell banking for themselves or a relative, 63% thought that stem cell banking would be useful to regenerate dental tissues. Most (89%) of the participants would be willing to save teeth and dental tissues for stem cell banking. These results suggest that endodontic practitioners are supportive and optimistic about the future use of REPs. (*J Endod* 2009;35:1204–1210)

Key Words

Dentin, pulp, stem cell bank, stem cells, tissue engineering

From the Nova Southeastern University, Fort Lauderdale, FL, USA.

Address requests for reprints to Dr Peter E. Murray, Department of Endodontics, College of Dental Medicine, Nova Southeastern University, 3200 South University Drive, Fort Lauderdale, FL 33328-2018. E-mail address: petemurr@nova.edu.

0099-2399/\$0 - see front matter

Copyright © 2009 American Association of Endodontists.
doi:10.1016/j.joen.2009.04.059

The American Dental Association has a Principles of Ethics and Code of Professional Conduct policy that applies to all its members (1). The guidelines do not address the issue of tissue regeneration and the use of stem cells as part of dental treatment. The lack of guidelines in this field is a cause for concern because endodontists, dentists, researchers, and the general public could be unsure or unaware of the ethical boundaries that should be applied to regenerative and stem cell therapies. The ethics and code of dental professional conduct must be updated to include guidance on new technologies and treatments that are controversial or potentially offensive, such as the use of stem cells therapies. An up-to-date principles of ethics and code of professional conduct are necessary to maintain the self-respect of the dental profession and the respect of the patients we serve (2). In order to establish the ethical guidelines, it is necessary to survey practicing endodontists about their attitudes toward regenerative endodontic procedures (REPs).

The first review of REPs defined them as biologically based procedures designed to predictably replace damaged, diseased, or missing structures, including dentin and root structures as well as cells of the pulp-dentin complex, with live viable tissues, preferably of the same origin, that restore the normal physiologic functions of the pulp-dentin complex (3). The term REP may include all treatments that accomplish pulp-dentin regeneration from the simplest blood clot revascularization method (4–7) to the most complex treatment, which involves creating tissue-engineered dental pulp constructs in the laboratory and implanting them into cleaned and shaped root canals (8). The blood clot revascularization method is the simplest method because it involves only one or two steps. The first step is to disinfect the pulp with a triple antibiotic paste (9); this step may be optional (10). The second step is to open the tooth apex to 1 mm or more to allow systemic bleeding into the canal (4, 5). This treatment was developed from the pioneering studies of Dr Nygaard-Ostby and his colleagues in the 1970s who reported new tissue formation in the root canal after total pulpectomy and partial root filling (6, 7). There is a growing body of evidence to show that this blood clot revascularization technique is successful, but so far the human data are limited to a few case reports and studies on traumatized immature teeth with incomplete root formation. The advantage of this method is that it has the potential to thicken the thin dentin walls of developing teeth (4–7), a feat not possible with current common root canal obturation treatments. The most complex REPs under evaluation involve the creation of dental pulp tissue constructs in the laboratory to be implanted into patient teeth (8). This procedure uses stem cells, growth factors, three-dimensional tissue engineering scaffolds, and tissue culture methods (8). The sourcing of stem/progenitor cells, body tissue, or DNA from the donation of teeth, tissues, blood, or bone marrow is controversial. The most ethical REPs may involve the use of a patient's own cells or body tissues.

There is no evidence in the scientific literature that provides information about the opinions, beliefs, and attitudes of endodontists regarding the delivery of potential REPs. It is important to understand the attitude of the endodontic community to this new era of treatments. The endodontists will be the first providers for REPs, and they will inform and educate the patient about new procedures. The aim of this survey was to collect the opinions of endodontists toward the use of REPs. The opinions are needed to help create ethical guidelines and to assess the potential acceptance of REPs among endodontic practitioners.

Materials and Methods

After Nova Southeastern University institutional review board approval, 100 copies of a questionnaire were circulated at the 2008 Endodontic College of Diplomates Summer Conference on the issue of REPs. Part A asked questions about the dentist's professional status. Part B asked questions about the dentist's opinions, beliefs, and judgments regarding the use of REPs, and part C consisted of questions based on current endodontic practice. The questionnaire was divided into three parts containing 40 questions. The questionnaire data were analyzed by the number of responses as a percentage of the total responses to gain an insight into the majority opinions of the participants.

Results

The overall response rate to the questionnaire was 56%. The completed questionnaires were obtained from 53 endodontists, one oral surgeon, and one general dentist attending the 2008 AAE Diplomates Summer Conference on the issue of REPs. Some participants gave more than one reply to each question or did not reply to each question. The questionnaire results are shown in Table 1.

Professional Status

Most of the participants were male (83.6%), the majority of the participants were older than 56 years of age (56.4%), and most of the participants had at least 21 years of experience (70.9%). The primary places of practice of the survey participants were in suburban areas (36.9%). Most participants read scientific dental journals every week (77.8%). More than half the participants had received continued education in stem cells and/or regenerative dental treatments (56.4%).

Ethical Opinions, Beliefs, and Judgments

The majority of participants thought that regenerative therapy should be incorporated into dentistry (96.4%). However, only a few participants (14.5%) had used umbilical cord or other types of stem cell banking for themselves or a relative. Almost two thirds of participants (63.6%) thought that stem cell banking would be useful to regenerate dental tissues. Two thirds of participants (63.6%) also thought that regenerative stem cell therapies will be used in dentistry within the next decade. Half the participants (47.5%) believe that it will be possible to implant new teeth grown in a laboratory in the next 11 to 20 years. Most of the participants (90.9%) were willing to attend training in REPs. The participants thought the greatest obstacles to a patient accepting REPs was a higher cost of treatment (58.2%) and a fear of stem cell therapy (30.9%). The majority of participants (84.5%) would agree to save teeth and dental tissue for use as part of future REPs. Half the participants (50%) thought that REPs could be a more successful treatment than implants, most of the others (46.3%) were unsure, and only two participants (3.7%) did not consider that REPs could be a better treatment than implants.

Fifty of the participants (87.9%) agreed that REPs should be tested on animals before clinical testing. More than half of the participants (50.9%) were willing to deliver embryonic stem cells sourced from a human fetus as part of dental treatment, 9 participants were unwilling to use these cells (15.8%), and 19 participants (33.3%) were unsure. The participants were equally divided over the potential of REPs to cause health hazards; 33.8% thought that health hazards could be produced, 30.8% thought that health hazards were not likely, and the remaining 35.4% were unsure. More than half the participants (52.3%) agreed that the dental professional associations should regulate the use of stem cell therapies; the remaining participants did not want regulation (24.6%) or were unsure (23.1%).

Clinical Practice

Half of the participants (49.1%) were already using some type of regenerative therapy in their practice, such as membranes, scaffolds, or bioactive materials; the remaining participants (50.9%) did not use any regenerative therapies in their practice. Most of the participants (55.1%) did not know if the outcomes of REPs would be successful; two participants (3.5%) thought it would be unsuccessful, and the remaining participants (41.4%) thought regenerative treatments would be successful. Two thirds of the participants (66.7%) did not know if the healing of periapical tissues could be enhanced by tissue engineering. The remaining participants (31.5%) thought the healing of periapical tissues could be enhanced by REPs, except for one participant (1.8%).

The participants regarded the most valuable applications of REPs to be for the continued root development in immature teeth (20.6%). Four (6.4%) agreed that this kind of treatment could be used for pulp tissue revitalization within a root canal, four (7.3%) thought that REPs could be used to replant avulsed teeth, and two participants (3.2%) considered that REPs could be used to heal periradicular bone. Forty participants (63.4%) considered that REPs could be applied to root development, pulp revitalization, and replanting avulsed teeth and to heal periradicular bone. Only one participant (1.9%) was unsure that REPs could be used for any of these treatments.

The majority of participants reported that necrotic immature teeth accounted for less than 10% of cases in their practice (90.7%). The majority of participants also reported that avulsed or traumatized teeth accounted for less than 10% of cases in their practice (98.1%). Periradicular lesions were reported to account for between 26% and 50% of all cases seen by the majority of participants (52.7%). The majority of participants (47.7%) considered the application of calcium hydroxide followed by a mineral trioxide aggregate apical plug and backfilling with obturation material to be the optimal treatment for necrotic immature teeth. Only a quarter of participants (27.7%) considered the application of tribiotic paste and pulpal regeneration to be the optimal treatment for necrotic immature teeth.

Half the participants (50%) were willing to deliver REPs for a fee. A small proportion of participants (5.7%) would only provide REPs if it increased their income. More than two thirds of participants (67.2%) would be willing to refer patients to a stem cell treatment center. Two thirds of participants (67.9%) would also be willing to collect dental tissue for stem cell banks. The majority opinion of the participants (37.2%) agreed that the most appropriate fee for collecting dental tissues for stem cell banking should be more than \$100 per patient. Almost as many participants (30.3%) would be willing to collect dental tissues for no fee. The majority opinion of the participants (27.8%) was that patients would be willing to pay \$100 per year for dental stem cell banking. The majority of participants (47.3%) thought that the cost of REPs should be equal to current treatment costs. Half the participants (49.1%) invested in new technology for their office within the past year. The majority of participants would recommend stem cell treatments and REPs to their patients if it was the most effective treatment option (57.1%).

Discussion

This is the first survey to collect data on endodontic practitioner opinions toward REPs. This is also the first survey of its type to question health care providers regarding their opinions of stem cell therapies and REPs. The survey provides evidence that endodontists want to be at the forefront of treatment development and are interested in procedures that regenerate tooth structure. Stem cell therapies and regenerative treatments have been under development since human embryonic stem cell lines were first isolated more than a decade ago (9).

TABLE 1. Survey of the Endodontic College of Diplomates Attitudes toward Regenerative Dental Treatments

| A. Professional status: | |
|---|----------------|
| 1. Which is your field in dentistry? | |
| a. Endodontists | 96.4% (n = 53) |
| b. Pediatric Dentistry | 1.8% (n = 1) |
| c. General Practitioner | 1.8% (n = 1) |
| 2. How many years have you been in practice? | |
| a. 0- 10 years | 7.1% (n = 4) |
| b. 11-20 years | 32.2% (n = 13) |
| c. More than 20 years | 69.7% (n = 39) |
| 3. Where is your primary place of practice located | |
| a. Rural | 5.3% (n = 3) |
| b. Urban | 35% (n = 20) |
| c. Suburban | 36.9% (n = 21) |
| d. Academic environment | 17.5% (n = 10) |
| e. Military | 5.3% (n = 3) |
| 4. What is your sex? | |
| a. Male | 83.6% (n = 46) |
| b. Female | 16.4% (n = 9) |
| 5. What is your age group? | |
| a. 25-35 years | 1.8% (n = 1) |
| b. 36-45 years | 14.5% (n = 8) |
| c. 46-55years | 27.3% (n = 15) |
| d. 56 or more | 56.4% (n = 31) |
| 6. Which is the most common payment plan used in your practice? | |
| a. Fee for service | 46.4% (n = 26) |
| b. Dental Insurance | 51.8% (n = 29) |
| c. Medicaid | 1.8% (n = 1) |
| 7. How frequently do you read scientific dental journals? | |
| a. Every week | 77.8% (n = 42) |
| b. Every year | 18.5% (n = 10) |
| c. Within the past 5 years | 0% (n = 0) |
| d. Never | 3.7% (n = 2) |
| 8. Have you ever received continued education in stem cells and/or regenerative dental treatments? | |
| a. Yes | 56.4% (n = 31) |
| b. No | 43.6% (n = 24) |
| B. Ethical opinions, beliefs and judgment: | |
| 9. Should regenerative therapy be incorporated into dentistry? | |
| a. Yes | 96.4% (n = 53) |
| b. No | 0% (n = 0) |
| c. Maybe | 3.6% (n = 2) |
| 10. Have you or any of your relatives used umbilical cord or other types of stem cell banking? | |
| a. Yes | 14.5% (n = 8) |
| b. No | 85.5% (n = 47) |
| c. Unsure | 0% (n = 0) |
| 11. Do you think that dental stem cell banking will be useful to be able to regenerate dental tissues? | |
| a. Yes | 63.6% (n = 35) |
| b. No | 5.5% (n = 3) |
| c. Unsure | 30.9% (n = 17) |
| 12. How many years do you think it will take for some regenerative stem cell therapies to be used in dentistry? | |
| a. 0-10 years | 63.6% (n = 35) |
| b. 11-20 years | 34.6% (n = 19) |
| c. More than 21 years | 1.8% (n = 1) |
| 13. How many years do you think it will take before dentists are able to implant new teeth grown in a laboratory? | |
| a. 0-10 years | 35.6% (n = 21) |
| b. 11-20 years | 47.5% (n = 28) |
| c. More than 21 years | 16.9% (n = 10) |
| 14. Would you be willing to attend a training course and/or continuing education courses to apply regenerative dental treatments? | |
| a. Yes | 90.9% (n = 50) |
| b. No | 3.6% (n = 2) |
| c. Unsure | 5.5% (n = 3) |
| 15. What do you think would be the biggest obstacle to a patient accepting regenerative dental treatment? | |
| a. Higher cost | 55.2% (n = 32) |
| b. Fear of stem cells | 29.3% (n = 17) |
| c. Other reasons | 15.5% (n = 9) |

| | |
|---|----------------|
| 16. Would you be willing to save teeth and dental tissue for future regenerative dental treatment? | |
| a. Yes | 84.5% (n = 49) |
| b. No | 0% (n = 0) |
| c. Unsure | 15.5% (n = 9) |
| 17. Do you think that regenerative dental treatment will be a better treatment option than tooth implant placement? | |
| a. Yes | 50% (n = 27) |
| b. No | 3.7% (n = 2) |
| c. Unsure | 46.3% (n = 25) |
| 18. Do you think stem cells and regenerate treatments should be tested on animals prior to clinical testing? | |
| a. Yes | 87.7% (n = 50) |
| b. No | 10.5% (n = 6) |
| c. Unsure | 1.8% (n = 1) |
| 19. Would you be willing to deliver dental treatments that involve embryonic stem cells sourced from a human fetus? | |
| a. Yes | 50.9% (n = 29) |
| b. No | 15.8% (n = 9) |
| c. Unsure | 33.3% (n = 19) |
| 20. Are you concerned about any potential health hazards regarding the use of stem cells as part of regenerative dentistry? | |
| a. Yes | 33.8% (n = 22) |
| b. No | 30.8% (n = 20) |
| c. Unsure | 35.4% (n = 23) |
| 21. Do you believe there is a risk that stem cell clinics will deliver future dental treatments? | |
| a. Yes | 25.9% (n = 14) |
| b. No | 29.6% (n = 16) |
| c. Unsure | 44.5% (n = 24) |
| 22. Do you believe that dental professional associations should regulate the use of stem cell and regenerative dentistry? | |
| a. Yes | 52.3% (n = 34) |
| b. No | 24.6% (n = 16) |
| c. Unsure | 23.1% (n = 15) |
| C. Clinical practice: | |
| 23. Do you use any type of regenerative procedures in your practice, such as membranes, scaffolds or bioactive materials? | |
| a. Yes | 49.1% (n = 27) |
| b. No | 50.9% (n = 28) |
| 24. What is your assessment of regenerative dental treatment outcomes? | |
| a. Successful | 41.4% (n = 24) |
| b. Unsuccessful | 3.5% (n = 2) |
| c. Don't know | 55.1% (n = 32) |
| 25. After nonsurgical root canal treatment, would the healing of periapical tissues be enhanced by tissue engineering? | |
| a. Yes | 31.5% (n = 17) |
| b. No | 1.8% (n = 1) |
| c. Don't know | 66.7% (n = 36) |
| 26. Which of the following regenerative endodontic treatments is the most valuable? | |
| a. Healing of periradicular bone | 3.2% (n = 2) |
| b. Continued root development in immature teeth | 20.6% (n = 13) |
| c. Pulp tissue revitalization within a root canal | 6.4% (n = 4) |
| d. Tooth re-implantation | 6.4% (n = 4) |
| e. All of the above | 63.4% (n = 40) |
| 27. What percentage of cases in your practice involves necrotic immature teeth? | |
| a. Less than 10% | 90.7% (n = 49) |
| b. 11%-25% | 5.6% (n = 3) |
| c. 26%-50% | 1.8% (n = 1) |
| d. More than 50% | 1.9% (n = 1) |
| 28. What percentage of cases in your practice involves avulsed or traumatized teeth? | |
| a. Less than 10% | 98.1% (n = 53) |
| b. 11%-25% | 1.9% (n = 1) |
| c. 26%-50% | 0% (n = 0) |
| d. More than 50% | 0% (n = 0) |
| 29. What percentage of cases in your practice involves periradicular lesions? | |
| a. Less than 10% | 0% (n = 0) |
| b. 11-25% | 16.4% (n = 9) |
| c. 26%-50% | 52.7% (n = 29) |
| d. More than 50% | 30.9% (n = 17) |

(Continued)

TABLE 1. *Continued*

| | |
|---|----------------|
| 30. What do you consider to be the optimal treatment for necrotic immature teeth? | |
| a. Calcium hydroxide apexification | 13.8% (n = 9) |
| b. Calcium hydroxide application followed by MTA apical plug and backfilling with obturation material | 47.7% (n = 31) |
| c. MTA apical plug and back-fill with obturation material | 10.8% (n = 7) |
| d. Tribiomatic paste and pulpal regeneration | 27.7% (n = 18) |
| 31. Using which payment plan would you be most willing to deliver stem cell and regenerative dental treatment? | |
| a. Fee for service | 50% (n = 32) |
| b. Dental Insurance | 15.6% (n = 10) |
| c. Medicaid | 0 |
| d. All of the above | 31.3% (n = 20) |
| e. None | 3.1% (n = 2) |
| 32. Would you only provide regenerative dental treatment if you are able to increase your income? | |
| a. Yes | 5.7% (n = 3) |
| b. No | 83% (n = 44) |
| c. Unsure | 11.3% (n = 6) |
| 33. In a case where you can't provide a regenerative treatment, would you be willing to refer your patient to a stem cell treatment center? | |
| a. Yes | 67.2% (n = 39) |
| b. No | 3.5% (n=2) |
| c. Unsure | 27.6% (n = 16) |
| d. N/A | 1.7% (n = 1) |
| 34. Would you be willing to collect dental tissue for stem cell banks? | |
| a. Yes | 67.9% (n = 38) |
| b. No | 1.8% (n = 1) |
| c. Unsure | 28.6% (n = 16) |
| d. N/A | 1.7% (n = 1) |
| 35. What should your fee be for collecting dental tissues for stem cell banking? | |
| a. Nothing | 30.3% (n = 13) |
| b. \$25 | 2.3% (n = 1) |
| c. \$50 | 11.6% (n = 5) |
| d. \$100 | 11.6% (n = 5) |
| e. More than \$100 | 37.2% (n = 16) |
| f. Unsure | 7% (n = 3) |
| 36. How much do you think your patients be willing to pay for stem cell banking? | |
| a. Nothing | 24.1% (n = 13) |
| b. \$100 per year | 27.8% (n = 15) |
| c. \$101-\$200 per year | 14.8% (n = 8) |
| d. More than \$200 per year | 11.1% (n = 6) |
| e. Unsure | 22.2% (n = 12) |
| 37. What should the cost for regenerative dentistry be? | |
| a. Equal to current treatment | 47.3% (n = 26) |
| b. More than current treatment | 41.8% (n = 23) |
| c. Less than current treatment | 3.6% (n = 2) |
| d. Unsure | 7.3% (n = 4) |
| 38. When was the last time you invested in the new technology (digital radiography, patient record keeping software, cone beam CT) for your office? | |
| a. Last year | 49.1% (n = 27) |
| b. Last 5 years | 43.6% (n = 24) |
| c. More than 5 years | 7.3% (n = 4) |
| d. Never | 0% (n = 0) |
| 39. What would make you most likely to recommend stem cell and regenerative dental treatments to your patients? | |
| a. If it is the most effective treatment option | 57.1% (n = 44) |
| b. It is safe and reliable | 33.8% (n = 26) |
| c. If it is the most cost-effective option | 9.1% (n = 7) |
| d. I would never recommend it | 0% (n = 0) |
| 40. Please write here any comments you wish to make related to the survey | |

The increasing numbers of REPs, stem cell therapies, and tissue-engineering articles published in scientific journals (11), presented at conferences, and research developments disseminated in news reports are likely a key factor in the high general enthusiasm of the survey participants for the incorporation of REPs into future clinical practice. Almost all of the participants thought that REPs should be incorporated into

dentistry, and most would be willing to attend training in REPs. Two thirds of the participants thought that regenerative stem cell therapies will be used in dentistry within the next decade. Half of the participants were already using some type of regenerative procedures in their practice, such as membranes, scaffolds, or bioactive materials, suggesting that many regenerative procedures are already in common use.

The anticipated removal of US restrictions regarding the medical use of human embryonic stem cells by the Obama administration will create new ethical dilemmas for researchers, practitioners, and patients (12). Nevertheless, less than one third of the participants thought the greatest obstacle to a patient accepting REPs were a fear of stem cell therapy. The safety and potential health hazards of the REPs would ultimately depend on the nature of the procedure. The anticipated greater cost of REPs was a much greater concern.

Treatments that involve the injection of embryonic stem cells from a human fetus may be considered to be among the most controversial of the potential therapies (13). However, more than half of the survey participants were willing to use these cells, and only a few would not use human embryonic cells. Very few of the participants or their relatives had used stem cell banking, but the majority was willing to save dental tissue themselves for future REPs. Only a quarter of the participants were worried that stem cell clinics will deliver future dental treatments. The use of the patient's own stem cells or body tissue would appear to be the most ethical treatment option, and disbelief among the participants that embryonic stem cell therapy will be used as part of REPs would explain the lack of concern on this issue. Animal testing alternatives and a reduction in the numbers of animals used for research have been implemented in response to public opinion against the use for animals for research (14). However, despite this trend, most of the participants agreed that REPs should be tested on animals before clinical testing.

It is estimated that 2 million tooth implants are placed each year in the United States (15). The increasing placement of implants may compete with some endodontic treatments and even REPs (15). Half the participants thought that REPs would be a better treatment option than tooth implant placement. In a recent retrospective study, it was found that 97% of 1.4 million endodontic cases remain successful after 8 years (16) and a greater than 90% of success or survival rates reported for endodontic treatments and implants (17,18). That high standard of success presents a challenge to tissue engineering researchers and practitioners. The majority of the participants would only recommend REPs if they were the most effective treatment option. The message from this survey for researchers developing REPs is that they will have to establish an evidence base that ensures endodontic professionals and patients that the proposed regenerative endodontic treatments are successful and as safe as the conventional endodontic treatments they are seeking to replace.

The participants regarded the most valuable applications of REPs to be for the continued root development in immature teeth. The majority of participants considered that REPs could have a valuable role in root development, pulp revitalization, and replanting avulsed teeth and to heal periradicular bone. Half the participants were willing to deliver stem cell and regenerative dental treatment for a fee. A small proportion of the participants would only provide regenerative dental treatment if it increased their income. More than two thirds of the participants would be willing to refer patients to a stem cell treatment center and collect tissue for stem cell banks. The majority opinion of the participants was that the fee for collecting dental tissues for stem cell banking should be \$100 per patient. The majority of the participants thought that the cost of REPs should be equal to current treatment costs.

The education, training, and continuing education of endodontists have adapted to keep pace with the demands of delivering new therapies (19). Endodontists who become involved in regenerative therapies have a moral and professional obligation to remain current and competent, yet there are few training programs in REPs. It is possible that new training or certification programs may be required in addition to existing training requirements, and these issues will place a greater academic burden on practitioners. It appears that the participants

expect to have to take new training programs, as almost all were willing to attend REP training courses.

Human tissues intended for transplantation have been regulated by the Food and Drug Administration (FDA) since 1993. In 2005, three new, comprehensive regulations went into effect that address manufacturing activities associated with human cells, tissues, and cellular and tissue-based products (HTCTP): (1) companies that produce and distribute HTCTP must register with the FDA, (2) criteria must be met for donors to be eligible to donate tissues and is referred to as the "Donor Eligibility" rule, and (3) the processing and distribution of the tissues are subject to the "Current Good Tissue Practices" rule. Together they are designed to ensure that sound, high-quality practices are followed to reduce the risk of tissue contamination and of communicable disease transmission to recipients. These rules are available at www.fda.gov/cber/tissue/docs.htm (20). Some practitioners and researchers may believe that obtaining patient informed consent for a treatment makes the delivery of that treatment ethical. However, patient informed consent is neither necessary nor sufficient for clinical research to be considered as ethical (21). A broad consideration of the fundamental philosophies underlying major codes, declarations, and other documents relevant to research with human subjects is needed to systematically elucidate a coherent framework for evaluating the ethics of clinical research studies (22). More than half of the participants agreed that the dental professional associations should regulate the use of stem cell therapies; the remaining participants did not want regulation and were unsure who should provide regulation. The creation of ethical guidelines for the use of REPs in addition to the FDA guidelines is needed to protect patients and health care providers.

Conclusion

The survey participants were generally enthusiastic about the introduction and usefulness of REPs. The pioneering nature of this survey prevented comparisons with the opinions, beliefs, and attitudes of endodontists and other health care providers. It is not clear if the same enthusiasm exists among dentists, physicians, and other health care professionals for the introduction of stem cell and regenerative therapies. More survey research among health care providers is necessary to determine ethical guidelines and to assess the potential acceptance and limitations of delivering stem cell and regenerative therapies to patients. The formulation of ethical guidelines for the use of REPs appears necessary in addition to the American Dental Association guidelines to protect patients and health care providers.

Acknowledgment

The authors gratefully acknowledge the assistance of the AAE College of Diplomates. This study was supported by a NSU Health Professions Division Research Grant.

References

1. ADA principles of ethics and code of professional conduct. American Dental Association. Pa Dent J (Harrish) 1993;60:27-30.
2. Christensen GJ. I have had enough!. J Esthet Restor Dent 2004;16:83-6.
3. Murray PE, Garcia-Godoy F, Hargreaves KM. Regenerative endodontics: a review of current status and a call for action. J Endod 2007;33:377-90.
4. Banchs F, Trope M. Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? J Endod 2004;30:196-200.
5. Chueh LH, Huang GT. Immature teeth with periradicular periodontitis or abscess undergoing apexogenesis: a paradigm shift. J Endod 2006;32:1205-13.
6. Horsted P, Nygaard-Ostby B. Tissue formation in the root canal after total pulpectomy and partial root filling. Oral Surg Oral Med Oral Pathol 1978;46:275-82.

7. Nygaard-Ostby B, Hjortdal O. Tissue formation in the root canal following pulp removal. *Scand J Dent Res* 1971;79:333–49.
8. Godlieb EL, Murray PE, Namerow KN, et al. An ultrastructural investigation of tissue-engineered pulp constructs implanted within endodontically-treated teeth. *J Am Dent Assoc* 2008;139:457–65.
9. Thomson JA, Itskovitz-Eldor J, Shapiro SS, et al. Embryonic stem cell lines derived from human blastocysts. *Science* 1998;282:1145–7.
10. Hargreaves KM, Geisler T, Henry M, et al. Regeneration potential of the young permanent tooth: what does the future hold? *J Endod* 2008;34:S51–6.
11. Hacker MC, Mikos AG. Trends in tissue engineering research. *Tissue Eng* 2006;12:2049–57.
12. Hutson S. Challenges anticipated in removal of stem cell restrictions. *Nat Med* 2009;15:3.
13. Jain KK. Ethical and regulatory aspects of embryonic stem cell research. *Expert Opin Biol Ther* 2005;5:153–62.
14. Knight DJ, Breheny D. Alternatives to animal testing in the safety evaluation of products. *Altern Lab Anim* 2002;30:7–22.
15. Garcia-Godoy F, Murray PE. Status and potential commercial impact of stem cell-based treatments on dental and craniofacial regeneration. *Stem Cells Dev* 2006;15:881–7.
16. Salehrabi R, Rotstein I. Endodontic treatment outcomes in a large patient population in the USA: an epidemiological study. *J Endod* 2004;30:846–50.
17. Doyle SL, Hodges JS, Pesun IJ, et al. Retrospective cross sectional comparison of initial nonsurgical endodontic treatment and single-tooth implants. *J Endod* 2006;32:822–7.
18. Iqbal MK, Kim S. For teeth requiring endodontic treatment, what are the differences in outcomes of restored endodontically treated teeth compared to implant-supported restorations? *Int J Maxillofac Implants* 2007;96–116.
19. Koshy S, Chandler N. Continuing professional education in endodontics in New Zealand. *N Z Dent J* 2003;99:104–6.
20. Available at: www.fda.gov/cber/tissue/docs.htm. Accessed June 23, 2009.
21. Strasser T, Gallagher J. The ethics of health communication. *World Health Forum* 1994;15:175–7.
22. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *JAMA* 2000;283:2701–11.