FEATURE

American Dental Association Foundation: Ongoing Research on Oral Health Care

Written by Brian Hoyle

Gary Schumacher, DDS, American Dental Association Foundation, Gaithersburg, Maryland, USA, discussed the Dr Anthony Volpe Research Center's accomplishments over nearly 90 years, which include development of calcium phosphate cement, tooth-colored resin composites, and calcium fluoride remineralization therapy.

Research on resin composites continues, reflecting such advantages as preferable aesthetics and bonding behavior, minimal invasiveness, and repair capability. Disadvantages of current composites include shrinkage during polymerization, polymer biodegradation by salivary components, bacterial colonization, fatigue and wear, and water sorption.

Research is focusing on bisphenol A glycidyl methacrylate–based and triethylene glycol dimethacrylate–based composites as a means of eliminating bisphenol A from dental composites and sealants. The aim is to eliminate potentially hydrolyzable ester groups, increase rigidity (ie, less shrinkage), optimize viscosity, and optimize hydrophilicity to increase adhesion to the tooth surface. Another goal is to develop a self-healing composite; that is, self-repair of microcracks would extend the life of composite restorations.

A third area of interest is the development of nanorods containing antimicrobial compounds. This so-called smart defense system would consistently deliver more antimicrobial agents to dental composites used in restorations, which would lessen the risk of infection.

Jeffrey J. Kim, DDS, PhD, American Dental Association Foundation, Gaithersburg, Maryland, USA, discussed the use of dental pulp stem cells (DPSCs) in regenerative dentistry based on 3D polymer scaffolds and efforts to reduce medication-induced xerostomia. The use of stem cells in tooth regeneration adds to the lengthy list of potential diverse applications—for example, repair of cardiac damage and traumatic brain injury, restoration of sight, spinal cord injury, diabetes, and various arthritic conditions.

The challenges faced in the use of stem cells for tooth regeneration are similar to other stem cell applications and include successfully differentiating the stem cells into the desired cell type, engineering the process to occur successfully in vivo, and overcoming host-mediated rejection. The challenge is compounded in the tooth, which progresses in development from an immature stage containing fairly homogeneous arrangement of necrotic pulp to the mature tooth that contains a coronal seal, mineral trioxide aggregate, and new pulp tissue. Furthermore, the region of new root consists of bone, periodontal ligament, and cementum.

There are other obstacles to stem cell tooth regeneration: the small dimensions of the canal/pulp space, exposure of the stem cells to noxious compounds during the irrigation and disinfection of the tooth interior, and the necessity to maintain cell signaling at the tooth apex, which is crucial for tooth development.

Dr Kim and colleagues have 2 research foci in their efforts to surmount these obstacles. The first is to achieve lineage-specific differentiation of DPSCs. While DPSCs can differentiate into secondary dentin, the reorganized material lacks organized dentin and dentinal tubules. Differentiation that more closely mimics the real condition is needed. As well, in the lower portion of the tooth toward the apex, the differentiation of DPSCs must yield nerve and blood vessels.

The researchers have designed a device called an airbrush, which extrudes nanofibers. In contrast to the more random arrangement of nanofibers obtained using the technique of electrospinning, airbrushing produces more ordered networks of parallel nanofibers. The resulting nanofiber networks of differing fiber diameter and density are compatible with different regions of the tooth and support region-specific DPSC growth and differentiation.

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Proteins, including collagen and fibrinogen, can be embedded throughout the fiber polymer to provide a niche for the attachment, growth, and differentiation of stem cells. Bone regeneration after tooth extraction, gingival regeneration directly on a damaged tooth, and pulp regeneration within the tooth are possible applications.

Dr Kim and colleagues are also exploring remediation of medication-induced xerostomia (dry mouth), which affects an estimated 20% of the population and 25% of those who take 1 or more medications. Xerostomia is difficult to diagnose; treatment for it is palliative at best, and it increases the risk of root caries and periodontal disease. The researchers have successfully developed a mouse model of xerostomia that features changes in submandibular gland branching morphogenesis and impaired development of blood vessels and epithelium. The model will be used to clarify the precise details of xerostomia and its prevention.

Diane R. Bienek, PhD, American Dental Association Foundation, Gaithersburg, Maryland, USA, discussed alveolar osteitis (dry socket), a painful complication of tooth extraction in which the blood clot that normally forms as protection of the exposed tooth socket is prematurely dissolved or lost, leaving the bone exposed to air, blood, fluid, or whatever else enters the mouth. The result can be an infection and severe pain. Reported incidence rates vary from 0.5% to 26%. The many purported risk factors include surgical experience and procedure time, tooth anatomy, smoking, alcohol use, oral hygiene, grinding of the teeth, age, sex, and sex hormones. The focus of all of these factors is the process of fibrinolysis, which normally limits the excessive formation of blood clots. In dry socket, excessive fibrinolysis may destroy the blot clot.

Understanding the pathology of dry socket has been hampered by the disparate findings of the individual studies, which each lack the statistical power to determine the significance of a risk factor. To more productively clarify the issue, Dr Bienek and colleagues undertook a meta-analysis of identified cases. The approach allowed a productive statistical assessment.

Analyzing 32 studies individually revealed a significant sex-related difference in risk of dry socket. A global analysis of all of the studies determined that in 84% of the cases, women had a significantly ($P \leq .05$) overall higher rate of dry socket than men. An individual assessment of 40 cases revealed a significant association between dry socket and oral contraceptive use in 12 cases. The global analysis revealed a higher overall rate of dry socket among oral contraceptive users in 80% of the cases (average difference, $7.9\% \pm 2.7\%$; $P \leq .05$).

Since the hormonal levels of estradiol can vary widely with time, the data were reanalyzed after oral contraception use was removed as a confounder. Even then, the global assessment determined that in 67% of the cases, women not using oral contraceptives were at heightened risk of dry socket compared with men (average difference for men, $-3.6\% \pm 1.3\%$; $P \leq .05$). Menstruation at the time of tooth extraction was linked with a lower risk of dry socket, although the small number of cases ($n = 9$) and the different definitions regarding menstrual cycle timing precluded any definitive conclusion.

The findings allowed a risk stratification of the occurrence of dry socket, which could drive more detailed studies. Dental surgeons should be cognizant that women using oral contraceptives at the time of tooth extraction may be at greatest risk of dry socket, with appropriate postsurgery monitoring and precautions put in place. Future plans include the identification of the threshold concentration of estradiol that is linked with an increased risk of dry socket.