



The nutrient canal of bone (Haversian Canal) surrounded by osteocytes.

Regeneration Redefined

Progressive research is pushing the boundaries on how tissue regeneration may be used in the future—from growing new teeth to creating new blood vessels. Michael K. McGuire, DDS, provides an update.

Q Tissue engineering is a concept that many dental hygienists may not be familiar with. What is tissue engineering?

A Tissue engineering brings together cells, natural or synthetic scaffolds, and specific signals to create new tissues. In dentistry today, we are using tissue engineering primarily to regenerate bone and soft tissue around teeth. In the future, we may be able to regenerate an entire tooth from cells harvested from tooth buds. A study done at Harvard University took cells from the third molars of pigs and used them to actually regrow tooth-like structures that have enamel, dentin, and cementum.¹ Certainly this kind of advancement is possible in the distant future. Dental implants are wonderful options for our patients today, but in the future we may be actually growing new teeth.

Q How has periodontal regeneration been attempted?

A We have attempted to regrow lost attachment around teeth in two basic ways. For years we have filled the defect in the bone with materials that create a scaffold, usually something inert like a bone mineral or synthetic like a ceramic material. The cells from the border of the bone defect grew up, over, around, and through the scaffold that then bridged and filled in the bone defect. The second approach is guided tissue regeneration (GTR). In this approach, the bone defect is sealed off from the surrounding tissues by a membrane that guides cellular growth. It keeps epithelial cells out and encourages proliferation of the periodontal ligament and bone to grow up the root surface, filling the defect. Both of these approaches were effective with small defects, but not very predictable in more challenging ones.

So over the past decade, we've looked at ways to jumpstart the body's ability to regenerate. This was accomplished primarily through bioactive molecules. These molecules recruit the cells from the boundary of the bone defect, cause them to differentiate, proliferate, and migrate—taking part in the regenerative process. The product Emdogain[®], an extracellular protein, and platelet derived growth factor (PDGF)—are bioactive molecules that I have worked with in studies. We just completed a clinical study in our office using PDGF. We were one of 11 different centers in the largest multicenter clinical trial ever done on periodontal regeneration using recombinant platelet-derived growth factor (rhPDGF). PDGF stimulates the body's ability to increase blood supply to the area. It also stimulates periodontal ligament and bone cells. The results are very positive. They show that when a certain concentration of PDGF is used our ability to regenerate intrabony defects improves.

Q Biomimetics is often mentioned along with tissue engineering. What is it?

A Biomimetics is a term frequently used interchangeably with tissue engineering, but there are subtle differences.

Biomimetics is the science of reconstructing or mimicking natural processes or tissues with the expectation that regeneration will follow. The best example in dentistry is what happens when we place enamel matrix derivative (Emdogain) on the root surface. With its application, we attempt to mimic the natural mechanism of tooth development with the expectation that regeneration will follow. The proteins attract the cells into the defect. They then attach to the root and create a new attachment apparatus consisting of bone, periodontal ligaments, and cementum just as when a tooth is formed.

Q Let's talk about the evolution of pocket reduction from resection to regeneration.

A For most of us, the late 1970s were the last days of the resective approach, where the only way to eliminate the pocket was to cut away tissue. In the mid '80s, the approach moved from resective to regenerative with the inception of GTR. Given the right patient, defect, and surgical technique, it gave us increased predictability over other techniques at the time. Early attempts at GTR used membranes that had to be removed in a second surgical procedure and later we used biodegradable membranes that did not have to be removed. In the future, we will probably use bioactive membranes that improve the predictability of regeneration even further.

Q What types of patients will have less favorable outcomes with tissue regeneration?

A Certainly regeneration is much more difficult to achieve in smokers, people with para-functional habits that are uncontrolled, and noncompliant patients who don't follow through with professional maintenance and don't practice good self-care. Diabetics are sometimes more difficult to treat because they don't heal well. Access in the mouth is also a must. The clinician must be able to thoroughly debride these defects. If a patient's mouth is tiny, it may prevent effective debridement.

Q What do dental hygienists need to be aware of when treating patients who have undergone regeneration?

A The typical post-operative schedule begins with an office visit 1 week after the surgery to review oral hygiene instructions. We want the patient to begin brushing and flossing, but only supra-gingivally at this point. The next appointment is about 1 month later where a supra-gingival dental prophylaxis is accomplished. A second supra-gingival prophylaxis is usually done 2 months later. Subgingival instrumentation or probing in the grafted area should not begin until 6 months following treatment.

Q Can tissue engineering be used to treat gingival recession?

A With recession, there are two possible goals. One is to prevent any further recession, usually through a soft tissue graft. Another is to cover the recession that already exists. When trying to cover the root, the height of the contour of the tissue interproximally dictates how much root surface you can cover. One of the challenges with any sort of graft is that you have to go to a remote surgical area to harvest tissue. This necessitates two surgical sites in the patient. Often, the donor sites are more problematic for the patient as far as soreness and more difficult for the clinician because of bleeding. A lack of donor tissue in the patient's mouth has been a longstanding problem. From the very beginning, periodontists have longed for an unlimited supply of donor tissue. Many different materials have been tried, from cadaver skin to freeze-dried skin to sclera from the eye, but most of the results have not been as favorable as using the patient's own tissue.

I am very excited about the role that tissue engineering may play in solving this problem. The first organ of the body to be successfully engineered from lab to accepted patient use is human skin. Currently there is a material available that takes fibroblasts from newborn foreskins. Approximately 250,000 square feet of tissue can be grown from one foreskin.² That's six football fields! It is grown outside the human body in a very sterile, controlled process and then it can be frozen or cryo-preserved. When it's needed, the tissue can be thawed and is then ready to use. When it comes back to life after thawing, it is more robust than it was before being frozen. The fibroblasts in the graft have surface receptors so they can talk to each other and to the native cells. They physiologically titrate the amount of growth factors, glycominoglycons, and matrix proteins—all of the necessary factors for regeneration of the host defect. We've used this material in two studies, one growing attached gingiva around teeth and another evaluating root coverage-type grafts.³

Q It sounds like there is great potential with tissue engineering.

A Yes, and we've just begun to scratch the surface. This particular material has been placed over infarcted hearts in animals and the material created spontaneous blood vessel growth around the infarcts.⁴ In periodontics, our limiting factor is the blood supply to the defect. If through these new techniques, we can grow blood vessels, then the rules of regeneration will need to be rewritten. You do have to walk before you run so we're using this material for fairly mundane applications right now, but the future is exciting.

Q What is tissue engineering's role in treating patients with open interproximal spaces?

A My colleagues and I are doing the only study in the world on regenerating papilla. We take a small 3 mm biopsy from the maxillary tuberosity area and send the tissue to a laboratory. In approximately 6 weeks, the lab grows enough cells from the biopsy for our use. Before the lab sends the cells back to me, it banks them, so that once the cell line is created, it can be cryopreserved. For example, I could take my daughter's 18-year-old fibroblasts and bank them so when she's 50 and having some sort of problem, we can use her 18-year-old fibroblasts.

To rebuild the papilla, we inject the deficient papilla with 6 to 8 million of the patient's own fibroblasts. Three different injections are given a week apart in an effort to expand the papilla and close the open interproximal space. We are following these patients for a year. Our patients are currently at the 4 month mark. It is a blinded study so I do not know the results, but I can tell you the patients are excited.

Q What else do you think the future holds?

A We are leaving behind passive approaches to therapy. In the future everything we do will be bioactive. This will broaden our scope of practice and, most important, improve treatment predictability for our patients. D

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