Barrier Membranes — Materials Review Part II

By Arun Garg, DMD

IN PART ONE OF THIS TWO-PART SERIES ON BARRIER MEMBRANE MATERIALS, A REVIEW OF different types of barrier membranes was discussed, along with a breakdown of various features of each barrier material type and a discussion of the clinical applications best suited to each. As discussed in last month’s issue, the restoration of structure and function of bone and periodontium has been aided significantly by these materials, which enhance selective cell repopulation and stimulate healing while preventing gingival epithelium and connective tissue from inhabiting the newly created bony space.

Part two of this segment on barrier membrane materials will cover the remaining resorbable materials in use today, including calcium sulfate, acellular dermal allografts, laminar bone membranes, among others, and will also discuss the microbiology associated with barrier membranes. Further, a review of the newer research on the topic, including the application of nanotechnology principles to membrane technology, will be addressed.

Calcium Sulfate

Calcium sulfate, also known as plaster of Paris, has been used after immediate implant placement as part of a bone graft around implants. Medical-grade calcium sulfate serves to stabilize clots and shield the area from unwanted epithelial tissue growth. One of the advantages of this medium is the ready supply of calcium directly on the site of bone regeneration in the early mineralization process. Dental Implantology Update has previously published research on this topic,1,2 and newer studies continue to reinforce the use of calcium sulfate as a relevant graft material in today’s arsenal, either alone or in combination with other materials. A 2009 study comparing three materials used as bone substitutes in extraction sites with dental implants noted no radiographic evidence of difference between the three materials at 24-months of follow-up. The other two bone substitutes included magnesium-enriched hydroxyapatite and heterologous porcine bone.3 In this particular study, implants were placed three months after bone...
In newer studies, bicomposites of calcium-sulfate based allograft containing demineralized bone matrix particles and other biologically derived products have been shown to have success as a graft material with safety and efficacy.\(^6\) A 2009 study out of Italy demonstrated histological and radiographic bone growth following maxillary sinus floor augmentation with immediate implant placement. The ratio between the original and grafted sinus height was computed and found to be significantly greater with the use of the bicomposite. Bone biopsies of the sites demonstrated histographic evidence of newly formed bone without inflammation.\(^6\)

Calcium sulfate has also been shown to facilitate wound closure when wound closure of the barrier membrane is not possible.\(^7,8\) An experiment comparing migration of human gingival fibroblasts along a chemotactic gradient over three different barrier membrane materials, published in 1996 in the Journal of Periodontology, demonstrated optimal results with calcium sulfate. In that particular study, polyacrylic acid and e-PTFE were used along with calcium sulfate and cell attachment, spreading, and mean migration distance were all compared. The results suggest that healing by secondary intention may be enhanced using calcium sulfate, especially in surgical sites where primary closure is unobtainable.\(^8\) Fifteen years later, scientists have recently published a report looking at cell motility and attachment on a titanium surface that has been modified, including one modification in which a titanium surface is roughened with calcium phosphate deposition.\(^9\) The authors are looking for selective means to attract osteoblasts to titanium to hasten osseointegration after implant placement, a common theme in dental implant-focused aspects of nanotechnology. The implication that different surface materials attract different types of cells is the premise of the study of nanotechnology, a field that, as discussed in previous issues of Dental Implantology Update, promises to revolutionize implant science. Biomaterials and other barrier membranes will certainly play a role in this arena.

Because calcium sulfate is an adhesive material, it obviates the need for sutures. The compound, on its own, dissolves in roughly 30 days without inflammatory reaction. It also does not attract bacteria or support infection; to further diminish chance of infection, many orthopedic surgeons use cement impregnated with antibiotic material in infected prosthetic replacements.\(^10-12\) In some, calcium sulfate offers the following advantages: complete resorption in 3-4 weeks, no increased inflammatory response, adaptability to the site, porosity (allowing of fluid exchange with adequate exclusion of epithelium and connective tissue), minimal postoperative discomfort, clot protection in earl healing, soft tissue growth over calcium sulfate, reduced biofilm formation, and minimal effect on cellular morphology.

### Acellular Dermal Allografts

Acellular human cadaver skin, which is obtained from tissue banks, is another type of bioresorbable grafting material. The material is de-epithelialized and has undergone decellularization to eliminate immunological rejection by the host and eliminate the need for immune suppression. Dermal allografts have been in use for the treatment of severe burns and are also in regular use as a barrier membrane for muco-gingival defects, formation of attached gingival tissue and for soft-tissue development around dental implants. When used as a barrier membrane, studies suggest a six-week resorption time, with complete and permanent incorporation into the surrounding tissue.\(^10\) Generally, dermal allografts are safe and promote normal wound healing with no inflammatory infiltration. Acellular dermal
allografts have found a niche in their use as root coverage in the treatment of gingival recession, lessening healing time given the absence of a donor graft site at the palate.

In terms of barrier membrane usages, acellular dermal allografts are easy to place and adapt, and have predictable resorption times. Their lack of cellularity is clearly advantageous in terms of immunological protection given the absence of major histocompatibility complex class I and class II antigens.

A 2009 animal study published in the journal Clinical Oral Implants Research reviewed radiographic, histomorphometric and clinical outcomes in dogs that received acellular dermal matrix as a barrier in guided bone regeneration in comparison with dogs that received a bio-absorbable membrane (glycolide and lactide copolymer).13 One dog was excluded from the study and the remaining six dogs were evaluated in terms of difference between width and thickness of keratinized tissue in the two groups. Essentially, the results were comparable in the two groups.13 A multitude of case reports with specific, discrete applications for the substance as a barrier membrane have been published. In one such case, published in the International Journal of Periodontics and Restorative Dentistry, authors Park and Wang describe the use of acellular dermal matrix, used as a barrier membrane in the reconstruction of non-space making buccal dehiscences associated with implant placement. In addition to utilization of a mucogingival pouch flap technique, sandwiched layering of mineralized cancellous and cortical bone graft, acellular dermal matrix was placed for barrier membrane purposes and the technique yielded significant height difference, as well as critical bone thickness augmentation with bone density equivalent to that of the surrounding native bone.14

Laminar Bone Membranes

Composed of freeze-dried human laminar cortical bone, this material has been used as a barrier membrane with relative success, comparable to other barrier membrane materials. Several studies have demonstrated this. In one study, laminar bone sheets were used as barrier membranes for guided tissue regeneration around implants for ridge augmentation.13 Still, laminar bone membranes are used less frequently than other resorbable materials.

Freeze Dried Dura Mater

This human tissue product harvested from cadavers has been studied internationally and nationally, and it is widely felt that it serves well as a material for guided tissue regeneration; still, there has been strong criticism of its use given the association of prion diseases like Creutzfeld-Jakob that are transmitted by foreign entities in the body can be fashion into a membrane-type entity, especially when used in conjunction with other grafting materials. This too proves to be a short-acting biologic barrier, and thus is ineffective against epithelial tissue invasion. Generally PRP barriers are resorbed within 10 days. It is most useful for its healing properties. Other membranes are often infused with PRP gel to enhance short-term tissue healing.

Uses of Barrier Membranes in Current Studies

A 2010 study from the United Kingdom looked at radiographic alveolar bone changes following ridge preservation with different grafting biomaterials and the use of barrier membrane to aid guided tissue regeneration. The authors acknowledge that osseous resorption and remodeling following tooth extraction led to a loss of alveolar ridge width within the first 3 months post-extraction.18 Comparing synthetic bone substitute vs. bovine xenograft, with bi-layer collagen used in both groups, the authors found relatively comparable results between the two groups in terms of radiographic alveolar bone changes.

A 2011 study out of Rome, Italy looked at deproteinized bovine bone mineral and collagen barrier membrane in combination with mandibular bone block grafts to reduce graft bone resorption during healing. The authors concluded that the addition of bovine bone mineral and collagen membrane over a mandibular bone block graft could minimize graft resorption during healing; however, there were more complications in the test group and differences were relatively slight.19

Microbiology of Barrier Membranes

Most foreign entities in the body can be susceptible to the formation of a biofilm, the early adhesion of bacteria that can cause local inflammatory changes, wound dehiscence, even systemic illness and septic shock. Failure of barrier
membrane procedures may be caused by bacterial-related complications resulting from early exposure of the site. In one study, Bacteroides fragilis, Streptococcus pnumiae, Prevotella intermedia, and Staphyllococcus intermedia were found at sites with prematurely exposed membranes (exposed at 1 week) on titanium-reinforced polytetrafluoroethylene membranes in primates. Visual cues to the exposure and microorganism overgrowth included redness, edema, and tissue slough.

In human subjects, especially those with aggressive periodontal disease, Porphyromonas gingivalis and Streptococcus mutans are common microorganisms that have been known to have strong affinity for barrier membranes. In vitro studies have demonstrated differential preferences of some bacteria to certain barrier membrane compounds; other research has concluded that in vitro studies are ineffectual given the vast array of other factors that affect microorganism adherence and colonization, such as host defenses and bacterial competition.

A 2003 study out of the Faculty of Dental Medicine in Israel looked at various oral bacteria and commercially used collagen membranes; authors Sela, Kohavi, Krausz, Steinberg, and Rosen found that proteolytic bacterial enzymes take part in the degradation of collagen barrier membranes used for guided tissue regeneration, which may explain negative clinical outcomes associated with their use in some cases.

A more recent 2009 study out of the same institution compared three different collagen barrier membranes exposed to the oral cavity in an effort to obtain an in vivo look at how barrier membranes survive the local oral microenvironment. The single-blind, parallel group controlled clinical trial recruited volunteers in which membranes (three in each patient) were placed in the mouths of subjects who were absent any sign of gingival inflammation at the outset of the study. Ten days after placement, the membranes were removed and evaluated for integrity. Of the three collagen barriers used (glutaraldehyde cross-linked membrane, non-cross-linked membrane, and ribose cross-linked membrane), the ribose cross-linked membrane appeared to be the most robust in terms of resistance to local degrading factors in the oral environment.

As newer materials carry more antimicrobial properties, the extent to which microorganism-associated negative outcomes exist remains to be seen. Conversely, development of more resistant strains of bacteria that are less susceptible to destruction by antimicrobial agents could also arise as antimicrobial products are used more ubiquitously in the medical environment.

Nanotechnology

Several articles describing the nan persp ective regarding the use of barrier membrane technology in dental science have demonstrated that the field is ripe with possibility. Opting for guided tissue regeneration using materials that have bone morphogenic properties (those that stimulate a response at the level of the osteoblast) is becoming more relevant as the field continues to evolve. One study looked at the level of the degree to which tissue cells penetrated nanofibrous structures while comparing rates of gene expression in those respective nanoenvironments. Qualities like water affinity, tensile extension rate, and tissue cell responses are being considered in the development of new barrier materials.

Conclusions

Selecting the appropriate barrier that is suitable in a clinic situation remains to the practitioner and is based on appropriates for the patient and the defect. In some clinical situations, use of certain materials may be contraindicated—such as the use of nonresorbable materials in sinus membrane tears. In other situations, such as when membrane exposure is possible, use of resorbable membranes is contraindicated. Because each material has its own advantages and disadvantages, the clinician should carefully review the material being used for each procedure to maximize success and decrease morbidity for that particular situation. Literature review on the topic is also important, especially to understand potential pitfalls or to identify novel applications of specific materials. And adequate skill and practice with each type of material is also especially relevant.

References

8. Payne JM, Cobb CM, Rapley JW, Killow WJ, Spencer P. Migration of human gingival fibroblasts over October 2010
Difficult Cases: Understanding Systemic Sclerosis

By Arun Garg, DMD, and Ghislaine Guez MD, MBA

Dental implant providers have been faced with difficult cases—individuals with systemic disease whose disease processes eventually cause oral manifestations that lead to the need for dental implants. This complex subset of patients, though rare in everyday practice, exists, and certainly has a host of mitigating factors that influence their care—like corticosteroid use, medical comorbidities, anticoagulation, relative or functional immunosuppression, and anatomical variation. A look at this disease process, dental considerations, and implant case reports in this patient population are described below.

Systemic Sclerosis

Systemic sclerosis (SSC) is a connective tissue disorder that is progressive in course, variable in affected patients, and thought to be mediated by an autoimmune process whose etiology remains unclear at the present date. The hallmark of this disease is diffuse fibrosis of the skin and internal organs. Organs most commonly affected are the skin, heart, kidneys, gastrointestinal tract, and the lungs. The disease is more common in women than men; and for these women, symptoms typically begin to appear in their reproductive years (typically ages 30-50 years). Estimates suggest that there are between 100,000 and 500,000 affected individuals in the
Pathogenesis of this disease incorporates three cardinal features including vasculopathy, cellular and humoral immunity, and progressive visceral and vascular fibrosis in multiple organs. As these features begin to affect related viscera, patients with the disease may complain of dysphagia, shortness of breath, atypical chest pain, nonproductive cough, joint pain and swelling, limitation of movement and weakness.

The disease is thought to have a slight hereditary component (with family clustering); despite this fact there is only a 5% concordance for systemic sclerosis in monozygotic twins. And, as mentioned, etiology of disease is poorly understood. Some risk factors have emerged, all of which are environmental; it is thought that some underlying immunologic process is at work in a specific subset of individuals and when exposed to a given trigger, these individuals develop the clinical presentation of disease over time. A list of these risk factors is outlined in Table 1. It should be noted that some rheumatologic, autoimmune diseases were thought to be caused by cosmetic enhancements that contained silicone; however, subsequent research has dispelled the claim that there was a link between breast implants and connective-tissue disease.

There is no single laboratory test that will demonstrate the presence of systemic sclerosis. In fact, laboratory confirmation of disease tends to be somewhat piecemeal, and varies with different aspects of the disease and different organs that may be affected (see Table 2). Referral to a rheumatologist is merited in anyone with clinical features of disease; typically, thorough work-up begins when a patient presents to an internist with Raynaud’s phenomenon and dermatologic alteration suggestive of systemic sclerosis.

Treatment is mostly supportive, with the goal of diminishing damage due to microvascular disease in the fingers, supporting the patient’s nutritional status in the setting of gastro-esophageal involvement and/or malabsorption, reducing blood pressure and limited pulmonary hypertension, and protecting the kidneys. Corticosteroids play a limited role in the treatment of systemic sclerosis, largely due to the fact that side effects of the medication may worsen other features of disease, especially susceptibility to infection and alteration of normal mucosal flora throughout the body. Immune modulators like methotrexate and cyclophosphamide may be used in specific circumstances and more advanced visceral and/or joint involvement.

**Dental Considerations**

For the dentist, typical physical exam findings in this disease include pinched nose, thin, atrophic lips with tight perioral skin, microstomia with limited mouth opening. Depending on the progression of disease and extent of oral care, teeth may be missing, plaque deposits may be abundant, and gingivitis and gingival recession may also be present. Xerostomia is also a
characteristic feature of this disease, as salivary glands are not excluded from fibrotic change. See Table 3 for a full list of physical exam features in this disease. In a thorough and comprehensive review article in Arthritis Care and Research, published in August of this year, authors Alantar et al. reviewed literature pertaining to systemic sclerosis and drafted a set of recommendations for care of the patient with oral involvement of the disease. The authors carefully describe the pathophysiology of oral disease. Unfortunately, many of the issues seen in systemic sclerosis compound the oral pathology of the disease. For example, esophageal dysmotility and subsequent gastroesophageal reflux disease tends to worsen xerostomia. Poor gastrointestinal absorption of specific vitamins, notably B9 and B12, worsen oral mucosal atrophy. Limited mouth opening worsens plaque formation, periodontal disease, and caries (as does xerostomia). Temporomandibular joint involvement can also be seen in this subset of patients, making mouth opening even more challenging. In advanced cases, mandibular bone resorption is described, the mechanisms of which are poorly understood but likely contributed to by the aforementioned issues as well as hypovascularity in the face of microvascular insult and subsequent osteonecrosis.

The most important aspect of dental care for patients with systemic sclerosis is routine prevention, namely, careful brushing, flossing and application of antiseptic gels along with regular visits for dental cleaning. Routine oral hydration and rinsing, used in conjunction with medications that stimulate the salivary glands (pilocarpine) can also be employed to combat xerostomia. Education is an important aspect of the process towards preventing further oral symptomatology. Oral physical therapy with stretching exercises is also relevant. Careful medication review in this patient population is essential, especially in light of the fact that many may have been prescribed bisphosphonates with concurrent steroid administration. Working in conjunction with the patient’s rheumatologist and/or primary care physician will help determine if and when dental extraction, if necessary, should occur to reduce the risk of osteonecrosis of the jaw associated with previous bisphosphonate use. In fact, most authors on the topic suggest an entire team dedicated to the treatment of these patients, including representation from dermatology, oral pathology, oral surgery, endodontology, prosthodontology and periodontology.

**Implant Considerations**

Before undertaking the decision to proceed with implant therapy in a

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**Table 3: Clinical features seen in patients with systemic sclerosis**

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<thead>
<tr>
<th>Organ System</th>
<th>Clinical Disease Findings</th>
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<tbody>
<tr>
<td>Systemic</td>
<td>Fever, Weight Loss</td>
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<tr>
<td>Skin</td>
<td>Erythema, Tightened, fibrotic skin; loss of normal skin folds</td>
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<td></td>
<td>Telangiectasias</td>
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<td></td>
<td>Ulcerations (especially at the fingertips)</td>
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<td>Calcinosis (subdermal deposits)</td>
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<td></td>
<td>Raynaud’s phenomenon</td>
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<td>Pigmentation or depigmentation</td>
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<td>Hair loss</td>
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<tr>
<td>Mouth</td>
<td>Xerostomia</td>
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<td>Microstomia</td>
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<td></td>
<td>Periodontal diseases: gingivitis</td>
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<td></td>
<td>Plaque, caries, missing teeth</td>
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<td></td>
<td>Mandibular resorption</td>
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<td></td>
<td>Mask-like facies in advanced disease</td>
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<tr>
<td></td>
<td>Pale, thickened buccal surfaces</td>
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<tr>
<td>Muscles and Joints</td>
<td>Tendon friction rubs</td>
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<tr>
<td></td>
<td>Loss of joint definition (due to inflammation), especially in the fingers</td>
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<tr>
<td></td>
<td>Tapering of the fingers with resorption of bone</td>
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<td></td>
<td>Joint deformity, contracture in severe disease</td>
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<tr>
<td>Gastrointestinal</td>
<td>Esophageal dysmotility</td>
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<tr>
<td></td>
<td>Dysphagia</td>
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</tbody>
</table>
patient with systemic sclerosis, a thorough understanding of the patient’s disease process and severity is essential. Microvascular disease can limit wound healing, xerostomia predisposes to bacterial overgrowth, and limited oral aperture makes regular cleaning and routine care more of a challenge. Relatively few case reports exist on the topic of osseointegrated implants in patients with systemic sclerosis,\(^7\)\(^1\) and follow-up is limited. Certainly, more work needs to be done in this area. Case reports share the conclusion that the need for disease sequelae to be controlled is essential if osseointegration is to occur successfully. Additionally, because of the progressive nature of the disease and uncertain oral course, some gradual combination of abutments, fixed partial dentures, or complete overdenture may be the optimal treatment strategy. In the early course of disease, microstomia may limit connection of abutments several months after the implant procedure despite successful osseointegration.\(^7\) Despite challenges, providing patients with appropriate oral care and a means to continue to maintain adequate oral function and mastication is of the utmost importance, especially in light of the high risk of malnutrition in this group of patients who also have numerous gastroenterologic complications.

References


