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BIOMATERIALS : A boon to Periodontal and Peri-Implant Regeneration

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Abstract: Different levels of periodontal disorders erode the periodontal attachment. In addition to stopping these diseases, we must concentrate on regenerating and replacing the tissues that have been lost. On the other hand, the integration with the soft tissues is crucial to the success of dental implants, which are regarded as a blessing in the history of contemporary dentistry. Regardless of the chosen material and design, a successful outcome can only be obtained with the healing of the soft tissue layer positioned between the implant and the bone. Numerous biomaterials and biological mediators have been developed for years in an effort to restore the injured tissues completely using less invasive methods. Several of them are cited in various articles and evaluations from different sources as being summarized here.

Keywords: Biomaterials, Periodontal regeneration, Peri-implant regeneration, Barriers, Biologics, Bone grafts, Gene therapy, Stem Cell Techniques, Three-Dimensional printing .

Introduction: The primary factor in tooth loss in adults is periodontitis, which results in the gradual degradation of tissues that support teeth (such as the periodontal ligament, alveolar bone, and cementum). In addition to the conventional prosthesis, dental implants are an attempt to repair this missing dentition. The propensity of bone and supporting tissue around the missing tooth site must be assessed prior to every implant insertion that the dentist plans. Peri-implantitis is a term used to describe an inflammatory condition that affects the soft tissues around implants and contributes to bone loss. [1]

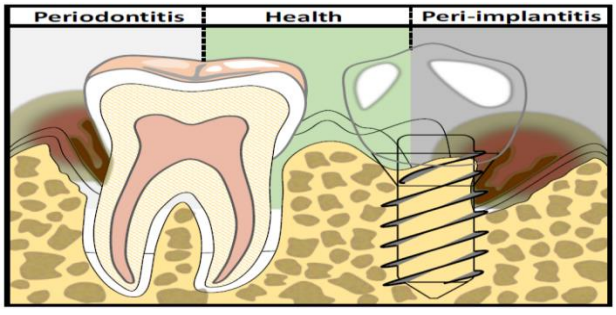

Fig 1: The image shows the progressive destruction of tooth-supporting structures in periodontitis and the inflammatory process in peri implants compared to that of a healthy tooth and a successful implant
Source: Local Oral Delivery Agents with Anti-Biofilm Properties for theTreatment of Periodontitis and Peri-Implantitis. A Narrative Review

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A regenerative strategy is necessary in a number of circumstances before or during the placement of the implant. With the ongoing development of tissue engineering, numerous biomaterials are proposed to improve periodontal and peri-implant regeneration outcomes.A treatment called periodontal and peri-implant regeneration tries to repair the harmed tissue surrounding implants and teeth.[1] Hard tissue regeneration, which included new bone production, mineralization, and osteoinduction, and soft tissue regeneration, which included growing interest in the prevention of periodontitis, peri-implantitis, and mucogingival diseases, have both produced positive results in recent years. [1]Stem cells, chemicals (growth factors), and biomaterials (scaffolds) are essential components if regeneration is to be successful and predictable[1].

The following biomaterials are currently being used:-

a) Bone grafts of different origin
b) Membranes for guided tissue regeneration
c) Growth factors
d) Stem cells

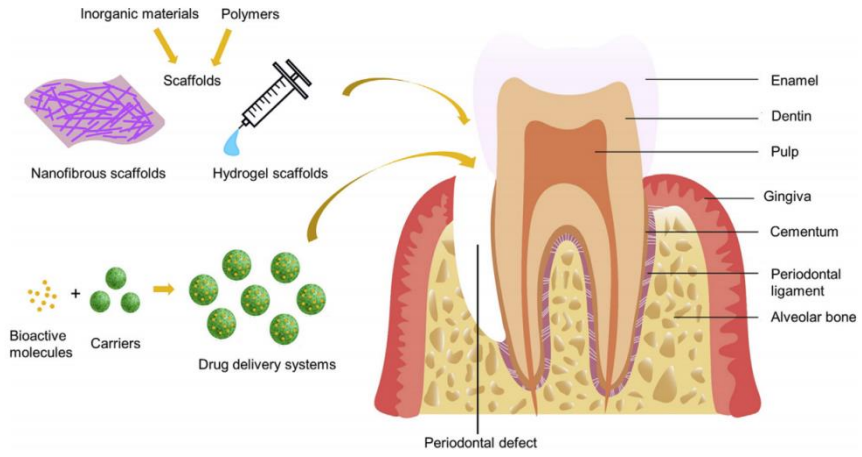

Fig2: Schematic illustration of the anatomy of periodontal tissues, periodontal defect, scaffolds of tissue engineering approach, and drug delivery system.
Source: Recent advances in periodontal regeneration: A biomaterial perspective

“ The regenerative medicine revolution is upon us. Like iron and steel to the industrial revolution, like the microchip to the tech revolution, stem cells will be the driving force of the next revolution.”

Similar to medicine and other closely connected fields including biomedical engineering, biomedical science, pharmacy, and pharmacology, dentistry has undergone a revolution as a result of the development of new technologies[2]. We have some newer forthcoming procedures, which are covered in this article, since the world as a whole is going forward with breakthroughs in every subject, including this field of Bio-Regenerations.

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Techniques of PERIODONTAL REGENERATION

- Guided Tissue Regeneration (GTR)
- TISSUE ENGINEERING

GTR is a regenerative surgical process that entails raising the mucogingival flap around the injured teeth, cleaning and smoothing the root surfaces, and temporarily putting barrier membranes under the gingiva. The technique's primary goal is to stop epithelium's apical expansion and cover the area above the denuded root surface with a barrier membrane, allowing PDL cells and osteoblasts to more easily produce PDL tissues and alveolar bone. [3]Greater clinical achievement level (CAL) gain, a decrease in probing pocket depth (PPD), and bone regeneration are a few advantages of GTR treatments.

The GTR treatment for periodontal regeneration has limits as well. One is that each individual case will have different regeneration effects from the GTR treatment. The outcomes of the GTR therapy are influenced by a number of additional variables, including diabetes, smoking, dental plaque control, tooth structure, and morphology. As a result, the results of GTR treatment may not always be favourable.

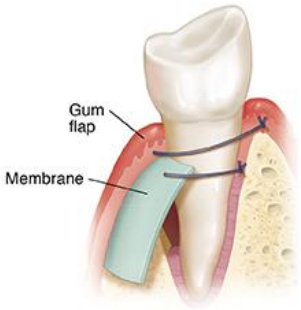

Fig 3; Guided Tissue Regeneration
Source: Periodontal Disease: Guided Tissue Regeneration (GTR) STAYWELL, HealthLibrary

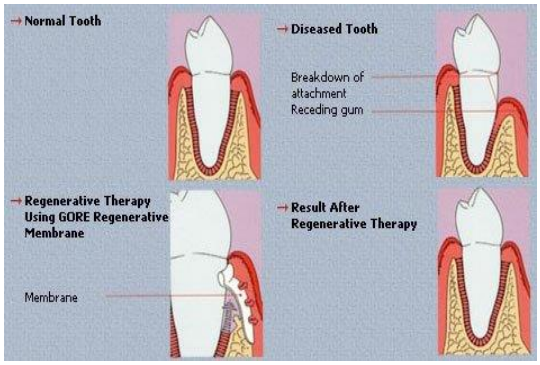

Fig 4:Guided Tissue Regeneration
Source: Guided Tissue Regeneration - Periodontal Implant Associates

The tissue engineering approach creates biomimetic systems to promote the creation of new tissues using stem/progenitor cells, scaffolds, and bioactive chemicals.

TISSUE ENGINEERING

- Scaffold-free approach
- Scaffold-based approach

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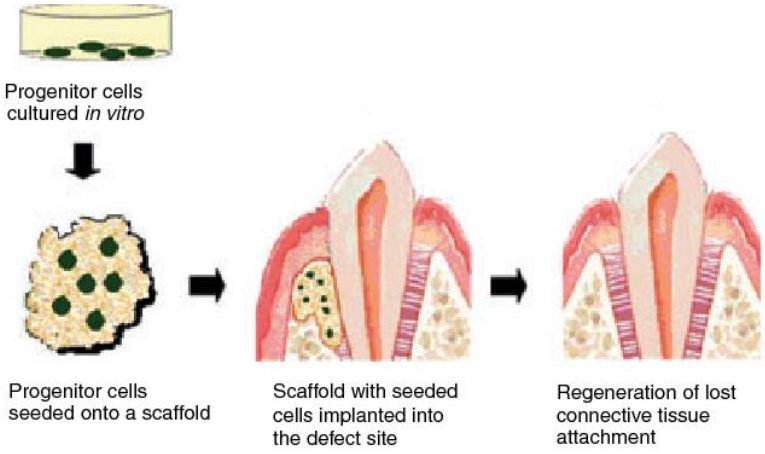

Fig5:Tissue engineering in Periodontal Regeneration.
Source: Stem cells and periodontal regeneration;N-HL in, S. Gronthos, P.Bartold

Scaffolding design for periodontal regeneration[3]

When creating a scaffold for periodontal regeneration, many criteria must be kept in mind. These include compositions, architecture, structure, and usability (injectability). In general, scaffolding materials should imitate the ECM microenvironment of the periodontium by having compositions that are identical to those of the ECM of periodontal tissues. Cementum, PDL, alveolar bone, and gingiva are all parts of the periodontium. [3] Each of the components has a unique design from the others.For instance, because alveolar bone is a hard tissue, the scaffold for alveolar bone regeneration should encourage the creation of mineralized tissue, whereas the scaffold for PDL regeneration should encourage the formation of soft tissue while preventing mineralization. Based on this, polymeric biomaterials are frequently employed for PDL regeneration whereas inorganic biomaterials, such as hydroxyapatite and calcium phosphate, serve as the scaffolding components to improve biomineralization. [8,9,10]

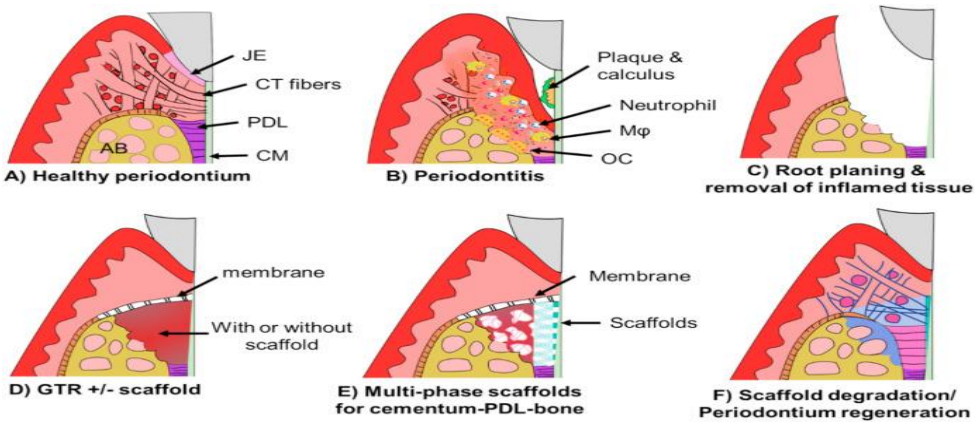

Fig6: Scaffold designing, Source: The recent advances in scaffolds for integrated periodontal regeneration

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TYPES OF BIOMATERIALS (depending on the mechanism of action)

1.**Barriers:** Materials called barriers are placed over periodontal defects to stop epithelial downgrowth. [1]

2. **Bones fillers:** Bone grafts or scaffolds called "bone fillers" are used to replace the missing alveolar bone.[1]

3.**Biologicals:** Growth factors, cell therapies, or medications that can be administered directly to the defect are biologics.

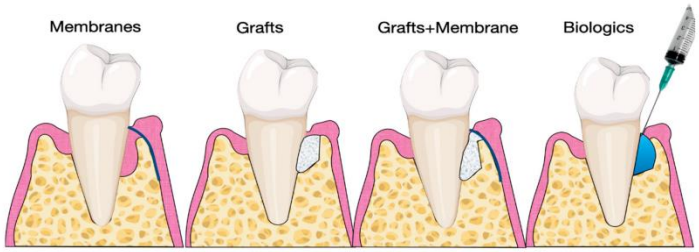

Fig 7: different biomaterials used in periodontal and peri-implant regeneration
Source : Periodontal Regenration byLeonardo Mancini ,Adrinao Franiti,Enrico Marchetti

FUNCTION OF BIOMATERIALS

a) Restore the alveolar bone proper
b) Providing adequate regeneration
c) Tooth stability
d) Soft and hard tissues around teeth and implants for clinical and esthetic reasons

TYPES OF BIOMATERIALS
ORIGIN

Biological/natural: By enabling good biocompatibility, biodegradability, an affinity for biomolecules, as well as strong wound-healing activity, natural biomaterials aid in the development of matrix-based regeneration approaches that aim to hasten clinical use. Scaffolds made of collagen, hyaluronic acid, alginate, and chitosan have long been employed in periodontal regeneration. [4] These materials' natural origins make it possible to create and engineer biomaterial systems that work at the molecular level, frequently reducing chronic inflammation. They may also be easily altered chemically and physically to take on specific forms, have desirable qualities, and carry out particular tasks for a variety of purposes. [4]

Synthetic: Scaffolding applications have frequently utilised a variety of synthetic polymers. In their natural state, synthetic matrices are devoid of cellular recognition sites. The benefits of synthetic polymers are numerous. They are biocompatible, can have their structural qualities controlled and reproduced, and can have their biodegradation rates customised for the desired purpose through precise chemical manipulation. A variety of fabrication techniques are used to create synthetic scaffolds, and these materials can be easily made into preset sizes and forms in accordance with therapeutic

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requirements. Depending on the mechanical and degrading characteristics of the specific application, synthetic matrices are often produced into solid scaffolds, tiny particles, or hydrogels[4].

SHAPES AND FORMS[1]

a) Granules
b) Particles
c) gel
d) 3D scaffolds
e) injectable substances
f) polymers
g) Matrices

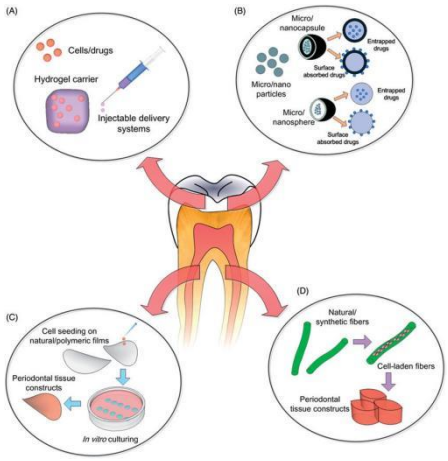

Fig 8: Schematic diagrams of developed biomaterials used for periodontal disease treatment. (A) Injectable hydrogels encapsulated with cells/drugs utilized for periodontal tissue repair. (B) Type of biodegradable micro/nanoparticles for periodontal drug delivery. According to the structural organization, biodegradable micro/nanoparticles are classified as micro/nanocapsules and micro/nanospheres. The drug molecules are either entrapped inside or adsorbed on the surface. (C) Natural/polymeric films seeded with PDL cells and in vitro cultured for periodontal tissue constructs. (D) Cells are seeded on natural/synthetic scaffolds and delivery of such scaffold-cell constructs for periodontal disease treatment.
Source: Advanced biomaterials and their potential applications in the treatment of periodontal disease; Xi Chen, Guofeng Wu; Zhihong Feng, Yan Dhong

BONE FILLERS

In order to help regenerate the lost or missing volume of periodontal defects, bone fillers are employed in ridge preservation or augmentation. The existence of a tooth or implant is crucial for regenerative potential.[1]

These are classified according to their ORIGIN

- Autografts
- Allografts
- Xenografts

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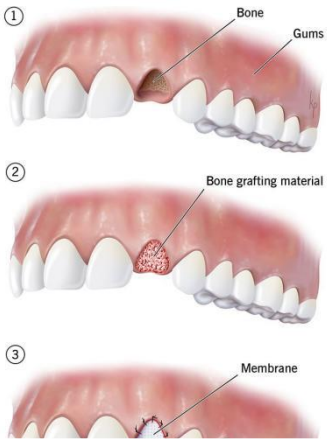

Fig 9: dental bone graft
Source: Cleveland Clinic

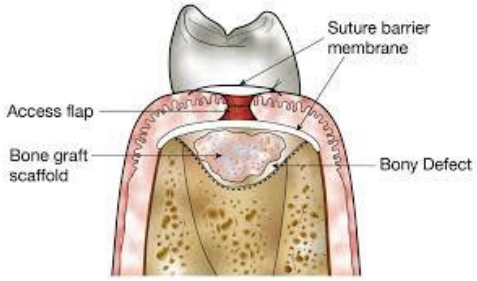

Fig10: Bone graft placement
Source; Bone Grafts and Substitutes in Dentistry: A Review of Current Trends and Developments

AUTOGRAFTS

History: NABERS and O'Leary made the initial autograft suggestion in 1965; they advised using cortical bone chips manually extracted from the surgical site.

Cushing proposed using ILIAC CREST in 1969 to induce the growth of new bone in the periodontium. [1] [5][6]

Uses: Due to their potential for promoting osteogenesis, osteoconduction, and osteoinduction as well as the lack of adverse reactions to foreign bodies, autografts are the gold standard, particularly for implant sites. Autografts are typically extracted intraorally from the extraction socket, edentulous ridge, symphysis, tuberosity, or buccal plate, depending on the size of a defect. However, if there are significant flaws, the process of harvesting is done from non-oral locations, such as the iliac, tibial, or cranial crests. [1][5][6]

Advantages: According to the needs of the recipient location, autogenous grafts can be obtained as cancellous, cortical, or combination grafts, and they have non-immunogenic properties, osteogenic potential, affordability, and the capacity to limit the risk of disease transmission. [1] [5] [6]

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Disadvantages: Autografts have a number of drawbacks, including donor site morbidity, second site surgery and the risk of potential complications, postoperative pain, lengthy operating times, and limited availability, making this approach less desirable for large sites and resulting in lower patient acceptance rates. [1] [5] [6]

ALLOGRAFTS

Allografts are genetically distinct biological materials taken from the same species. They could be mineralized, demineralized, fresh, frozen, or freeze-dried (lyophilized). In the process of extracting tissue, tissue banks are involved. Depending on the therapy, it may be possible to get freeze-dried bone (FDBAs) or decalcified freeze-dried bone (DFDBAs) [1] [5] [6]

Although certain allografts also have osteoinductive qualities, the majority of them are osteoconductive. Bone morphogenic proteins (BMPs), useful molecules in bone regeneration, are made visible by the allograft's decalcification.

[1] [5][6]

Advantages: Allografts provide a number of benefits, such as a lack of donor site morbidity, elimination of the donor site, shorter operating timeframes, and a wide variety of grafting medium configurations. [1][5]

Disadvantages: The inability to transplant osteoprogenitor cells, foreign body reactions, patient reluctance to have cadaveric bone grafts due to the risk of disease transmission, the fact that the majority of allografts lack significant osteoinductive capability, and high cost are all disadvantages of allografts. [1] [5]

XENOGRAFTS

Xenografts are bone substitutes that are transplanted into humans from other animals, such as BOVINE or PORCINE grafts.

The Geistlich Bio-Oss® particles (Geistlich Pharma, Wolhusen, Switzerland), which are harvested bovine and are regarded as a global reference product in oral regeneration, are just one of the commercial items that have been suggested based on this methodology.

[1] [5][6]

Advantages: One surgical operation, simple accessibility, and less patient morbidity are benefits of xenografts.

[1] [5]

Disadvantages: Due to their antigenicity, which is a drawback, these tissues must be thoroughly processed to eliminate the organic components. [1]

Compared with allografts, xenografts are reported to have increased connective tissue growth, delayed vascularization, and slower rates of resorption.

Table 1. Commercialized bone substitutes and heating temperature according to their production process and the manufacturing protocol.

Commercial Name	Sources	Heating Temperature
Bio-Oss®	Bovine	300 °C [38]
Re-bone®	Bovine	−80 °C to 121 °C [41]
Endobon®	Bovine	900 °C [42]
cerabone®	Bovine	1250 °C [43]
creos™	Bovine	600 °C [44]
PepGen P-15®	Bovine	1100 °C [45]
SmartBone®	Bovine + Porcine	50 °C < [46]
Gen-Os®	Porcine	130 °C [47]
Zcore®	Porcine	500 °C to 620 °C [48]
THE Graft™	Porcine	400 °C [49]
Equimatrix®	Equine	N/A
Bio-Gen®	Equine	130 °C [50]

Fig 11: Commercialized bone substitutes and heating temperature according to their production process and the manufacturing protocol. Source: Biomaterials for Periodontal and Peri-Implant Regeneration[1]

Barriers: Barrier membranes are utilised to stop the proliferation of epithelial cells and give room for PDL and alveolar bone to repair. Such qualities as biocompatibility, cellocclusiveness, tissue integration, space maintenance, and clinical manageability should be present.

Therefore, barriers are employed to restrict and select cells, enabling the regeneration of a particular tissue like bone or PDL, decreasing the downgrowth of epithelial cells in the defect, and preventing the creation of a lengthy junctional epithelium.

Barriers maintain the space of the defect, facilitating cell replication and tissue regeneration[1]

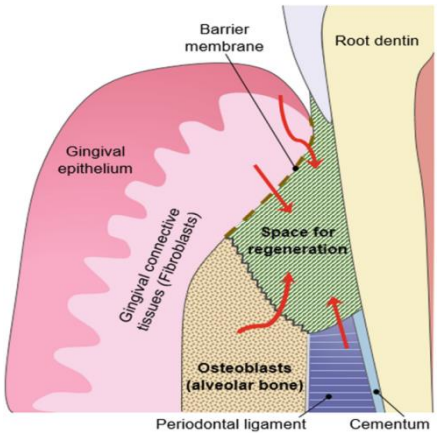

Fig12: the figure above describes the placement and function of a barrier membrane in periodontal regeneration. Source: Tissue Engineering in Periodontal Regeneration [12]

TYPES

a) Resorbable / Absorbable
b) Non-resorbable/ Non-Absorbable
c) Semi Absorbable

BASED ON ORIGIN

i. Autogenous
ii. Xenogeneic
iii. Allogenic
iv. Alloplastic

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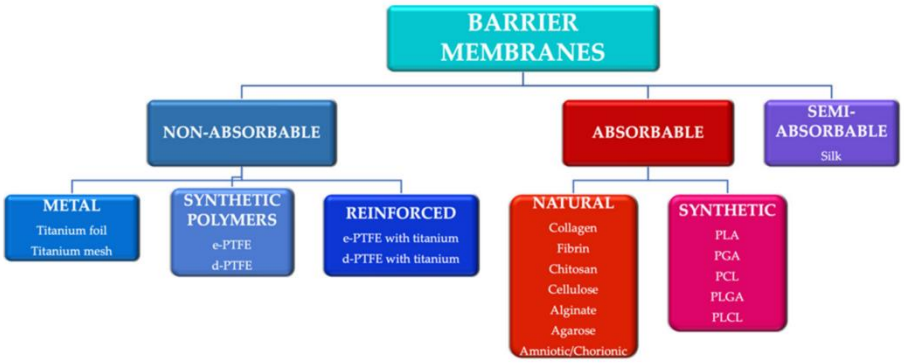

Fig 13: Types of Barrier Membranes
Source: Finding the Perfect Membrane: Current Knowledge on Barrier Membranes in Regenerative Procedures: A Descriptive Review

Since the first membrane based on cellulose acetate was employed in 1980, various materials have been created and researched.

RESORBABLE /ABSORBABLE BARRIERS

When compared to non-absorbable barriers, absorbable membranes don't require additional surgery after implantation and break down in vivo. There are two types of absorbable barriers: natural and artificial. Generally speaking, absorbable membranes have a lower mechanical strength than non-absorbable membranes.[1][4]

POSITIVE FACTORS

a) Reduction in patient discomfort

b) Bioactive properties

c) Ease of handling

NEGATIVE FACTORS

a) Unpredictable resorption pattern related to the degradation process

b) Presence of inflammation related to the degradation process.

RESORBABLE BARRIERS

A. NATURAL

Natural biomaterials have excellent biocompatibility with cellular binding sites, but have low mechanical strength with an unpredictable resorption pattern.[1][4]

The most used and widespread isthe collagen harvested, from animals. Type I collagen is responsible for theattraction and activation of PDL cells and fibroblasts.Thus, it is one of the most used for membrane production.

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B. SYNTHETIC

The mechanical resistance and predictable degradation of synthetic barriers can be tailored to the manufacturing process. but are not biologically recognised. The ability to maintain space and form new tissue is impacted by membranes' ability to degrade. The degradation rate should generally be moderate because fast degradation causes premature mechanical loss while slow degradation inhibits the growth of new tissue. [1][4]

NON-RESORBABLE BARRIERS

Generally speaking, non-absorbable membranes maintain space better than absorbable membranes. In the past ten years, titanium-reinforced membranes and polytetrafluoroethylene (ePTFE) have been the most often used materials. Gore-Tex (W. L. Gore & Associates, Inc., Newark, Denmark) created PTFE in 1990. The unique feature was the existence of a double layer with two distinct roles; the porous first layer seeks to encourage cell growth, while the other side serves as a space provider to prevent epithelial cell down growth. [1] [4]

In comparison to the PTFE membrane, the titanium-reinforced PTFE membrane had better results since it had a higher compressive strength. The titanium-reinforced PTFE membrane was extremely thin (0.01 mm), which allowed for more area for the development of new tissue[1]. [4]

After three months of healing and periodontal regeneration, several randomised clinical trials revealed intriguing findings. Others noted a number of issues (exposure, suppuration, and pain), which were presumably caused by how the flap was handled and the suture collapsing.

Due to the development of minimally invasive techniques, these barriers are no longer used (minimally invasive surgical technique, single flap approach, or modified minimally invasive approach).[4] Furthermore using these methods. It is challenging to handle a membrane. Nonabsorbable barrier membranes must also be removed via a second procedure, which worsens the results of regenerative surgery by posing a danger of infection and delaying wound healing. [4]

NON-RESORBABLE/ NON-ABSORBABLE BARRIERS

POSITIVE FACTORS

i. High mechanical stability
ii. Cell’s migration inhibition

NEGATIVE FACTORS

i. Second surgical intervention possible exposure
Ii. Accentuated inflammation in case of infection

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BIOLOGICS

a) Biological mediators are considered the last innovation in oral regeneration.
b) It is possible to classify these mediators in stem cells, growth factors, and gene therapy.
c) The most used and widespread are platelet-rich growth factors (PDGF), bone morphogenetic proteins (BMP), and enamel matrix derivatives (EMD)[1]

PLATELET-RICH GROWTH FACTORS (PDGF)

There are five isoforms of platelet-derived GF (PDGF), a serum GF for fibroblasts (AA, AB, BB, CC, and DD). Numerous studies have demonstrated the role of PDGF, which largely aids in wound healing, in promoting PDL cell proliferation and migration. [1][4]

It was discovered that PDGF-BB was more effective than the other isoforms at encouraging PDLC mitogenesis.A higher dose ($50 ng/mL) is needed for the attachment of PDL fibroblasts to damaged roots; concentrations of 5–20 ng/mL were ineffective. In vitro investigations revealed that PDGF-BB enhanced the proliferation of fibroblasts and osteoblasts at concentrations of 10–20 ng/mL. Additionally, studies on animal models and patients with periodontal disease have shown that PDGF is effective when combined with either IGF or dexamethasone, the latter of which is a well-known osteogenic differentiation factor. This is demonstrated by significant bone filling after reentry into the defects. [1] [4]The most used and analyzed product is GEM 21S®,(Osteohealth, Shirley, NY, USA) with in vivo and in vitro studies[1][4]

BONE MORPHOGENETIC PROTEINS (BMP)

A single molecular species of bone morphogenetic proteins (BMPs), such as BMP-2 or BMP-7, which are widely distributed in bone tissue and produced by a variety of cells, including osteoclasts and osteoblasts, is what triggers the bone-healing process. [1] [4].They initiated a series of biological processes that caused progenitor cells to differentiate into phenotypes involved in periodontal regeneration.According to recent research, the allograft proteins BMP-2, BMP-4, BMP-7 (also known as osteogenic protein-1, or OP-1), and BMP-12, which are frequently contained in allografts and exhibit osteoinductivity and influence cells' behaviour in bone regeneration, are strong inducers of bone formation during mandibular reconstruction, with OP-1 (rarely BMP-2) inducing significant cementogenesis. [1] [4]

In this situation, BMP-12 prevents ankylosis and root resorption after tooth replantation and supports the restoration of the PDL, including regeneration of cementum and functionally orientated fibres. [4]

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The effects, however, are optimum and are influenced by a variety of variables that require careful consideration in clinical research. We also need to be mindful that there have been reports of serious adverse effects such ankylosis and root resorption.

The high cost of synthetic manufacturing and the capacitation limit in synthetic biomaterials are further drawbacks to the extraction of BMPs.[4]

ENAMEL MATRIX DERIVATIVES (EMD)

In its original form—purified acid—a Swedish firm (Biora, Malmö, Sweden) issued the genuine and distinctive EMD derivatives that were taken from pig enamel in 1996.

In order to induce cell proliferation, migration, adhesion, mineralization, and differentiation in periodontal tissue, EMD, an extract of porcine immature enamel matrix, is regarded as a suitable protein mixture. Amelogenin makes up more than 95% of EMD, with very minor levels of enamelin and other proteins. [4]

The benefit of EMD is the mimic effect, which can draw cementoblasts to create new root cementum and therefore make it easier for a new periodontal ligament to grow. Since its introduction to the market in 1997, this product has received attention for its ease of use and intriguing periodontal regeneration results. EMD proteins, which are located on the root surface and are released by Hertwig's cells during the development of teeth and periodontal tissue, have an impact on the early stages of cementum, alveolar bone, and periodontal ligament formation. [4]

The name of the distinctive enamel derivatives on the market is Emdogain® (Straumann AG, Basel, Switzerland), which Straumann AS later purchased. It primarily consists of amelogenins. [1] [4]

Since Emdogain (Institut Straumann AG, Basel, Switzerland) has been approved by the US Food and Drug Administration (FDA) and is currently being used in clinical trials to determine its effectiveness, various clinical trials have been conducted.

[1] [4]

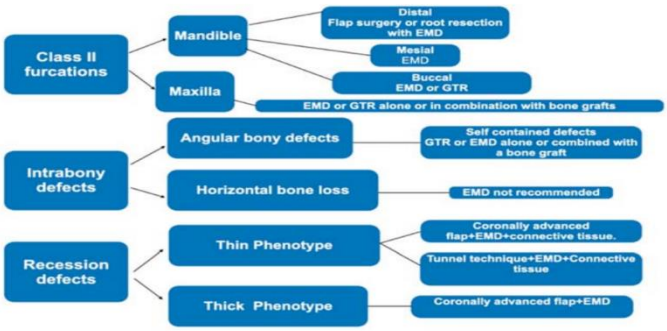

Fig 14: Clinical indications for EMD in periodontal regeneration concerning the defects' type

Source: Miron, R.J.; Sculean, A.; Cochran, D.L.; Froum, S.; Zucchelli, G. Twenty years of enamel matrix derivative: The past, the present and the future. J. Clin. Periodontol. 2016, 43, 668–683. [CrossRef] [PubMed][13]

Fig 15: Application of Emdogain
Source: Brooklyn Periodontics and Implant Dentistry, Sheldon Lu DMD

HYALURONIC ACID

A naturally occurring glycosaminoglycan called hyaluronic acid (HA) is found in many tissues, including connective tissue. It is a top-notch scaffold for gum tissue regeneration. Additionally, it appears to be antibacterial and anti-inflammatory[1]. The viscoelastic behaviour and ability to absorb a sizable amount of water are the main characteristics that make this a potential biomaterial .[1] Hydrogels contain hyaluronic acid as one of their constituents.

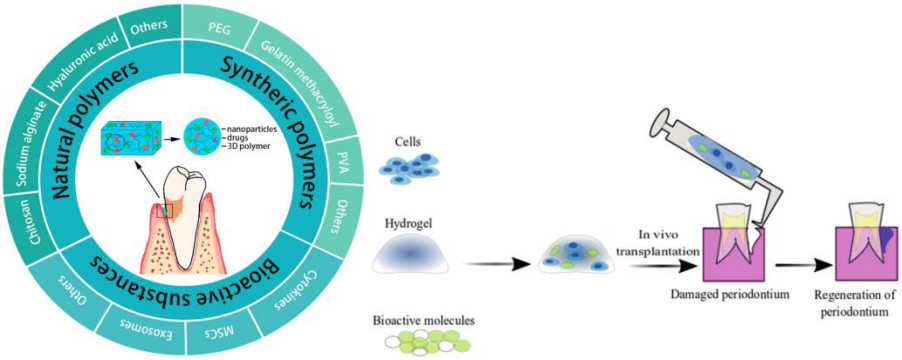

Fig 16: Hydrogels and their applications
Source: Advances of Hydrogel Therapy in Periodontal Regeneration

AUTOLOGOUS PLATELET CONCENTRATES (APG)

APGs are potential biomaterials for the regeneration of the peri-implant and periodontium. Platelet fibrin and growth factors, such as PDGF, vascular endothelial growth factors (VEGF), and transforming growth factors beta (TGF-b), which are classified as natural living cell scaffolds, make up the majority of the composition. [1]

Advantages

Autologous origin and the fast and chip protocol

Disadvantages

i. Handling and production
ii. fast resorption pattern that was estimated to be between 14 and 20 days

GENE THERAPY

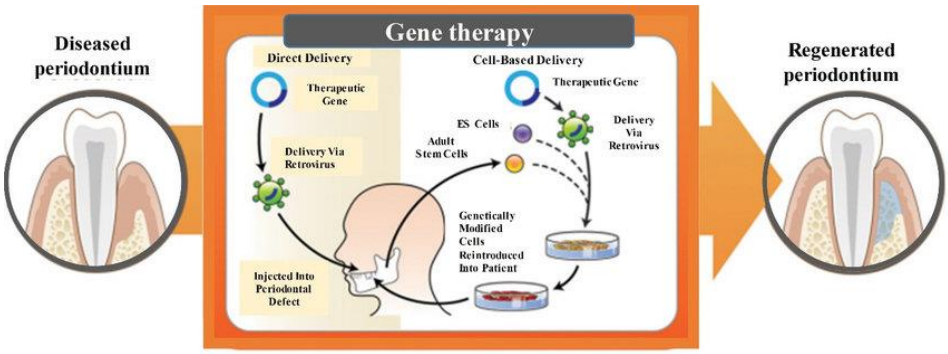

Fig 17:Gene therapy ;

Source: Gene Therapy-Future in Regenerative Periodontics

E. Rathi, Raja Babu, Harinatha Reddy
Published 2015
Medicine, Biology

Due to the limited in vivo half-lives of topically applied GFs, which typically range from a few hours to a few days, researchers have attempted to prolong protein activity by utilising gene delivery techniques that include turning cells into factories that produce protein. This is accomplished by either directly introducing plasmid DNA encoding the desired GF(s) into the cells or tissues, or by using gene delivery vehicles or vectors[11]. This novel idea has arisen as a potentially effective method for controlling the host reaction brought on by the periodontal microbe and the regeneration of periodontium throughout the course of the disease[7].

Cells can be altered in vitro by viral vector transduction, and when transplanted into patients, these cells may return normal tissue function. The combination of naked DNA and a biodegradable carrier, however, is the basis of one of the most promising gene therapy strategies for periodontal regeneration. By using collagen or other biomaterials, a so-called gene-activated matrix can be created that can transmit bare DNA that instructs a person's cells to have a therapeutic effect[7].

Instead of carrying and delivering altered stem/progenitor cells, a gene therapy product can instruct the existing cells to develop into a type more suited to the regenerative process [7].

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EMERGING TECHNIQUES

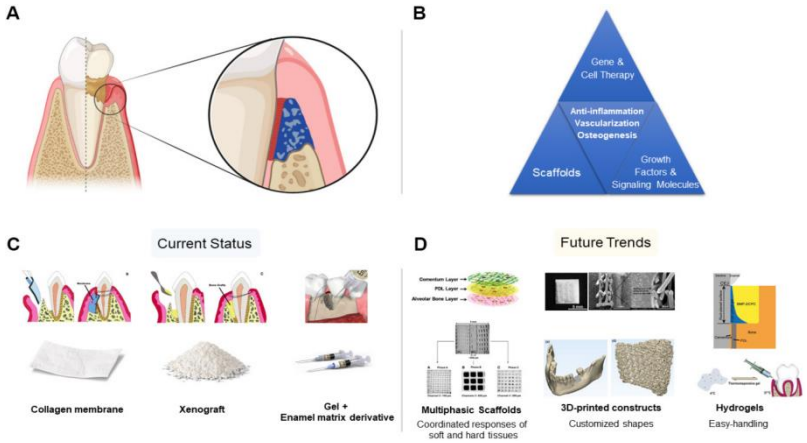

Fig 18: Current and future trends in periodontal tissue engineering and bone regeneration
Matthew Galli, Yao Yao1, William V. Giannobile, Hom-Lay Wang

STEM CELL TECHNIQUES

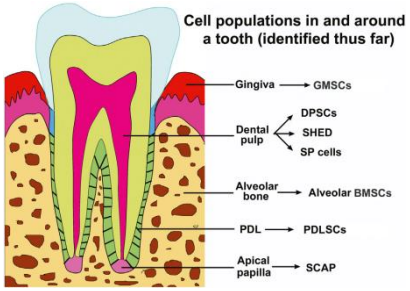

FIG19: Selected stem/progenitor cells identified thus far inand around a tooth.
Source: Periodontal tissue engineering and regeneration: Xiao-Tao He, Rui-Xin Wu, and Fa-Ming Chen[4]

Human body cells known as stem cells are self-renewing and have the ability to differentiate into any type of cell in an organism. They are initially unsophisticated, but as they evolve, they take several routes to specialisation.

Only when the root is developing before the tooth emerges into the oral cavity does the apical papilla tissue appear. The terminals of developing tooth roots contain SCAP, a distinct population of dental stem cells.

Dentine and PDL were created by inserting SCAP cells to create a root and PDLSC to create a PDL into the tooth sockets of mini pigs. However, because roots develop postnatally, the root apical papilla is accessible in dental clinical practise from excised wisdom teeth. The majority of early-stage human tissues are not clinically available for stem cell isolation. Thus, it is simple to obtain a very active pool of stem cells with characteristics similar to those of an embryo. [4]

The regeneration of cementum or periodontal ligaments using periodontal ligament stem cells (PDL-SCs). Alveolar bone and root surfaces also contain them, albeit the PDLSCs on the alveolar bone exhibit higher differentiation capabilities. In vitro, PDL-SCs can develop into mesenchymal cell lineages to produce adipocytes, osteoblast-like cells, cementum tissue, Sharpey fibres, and collagen-forming cells.

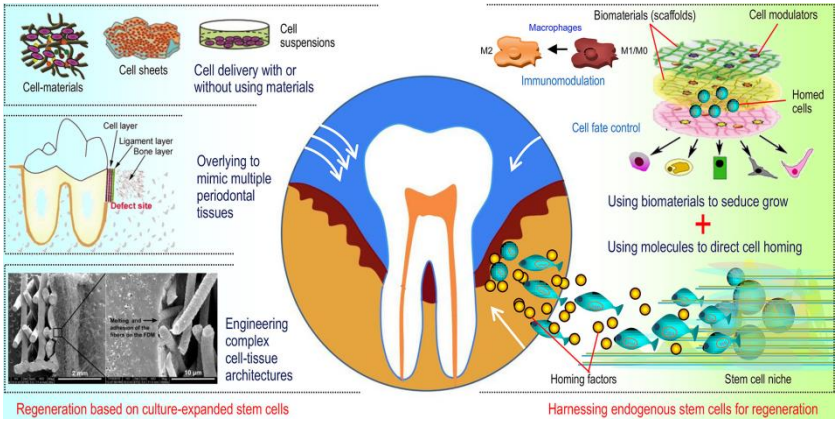

Fig20: Stem cell application in Periodontal regeneration and Peri-Implant Regeneration Source: Concise Review: Periodontal Tissue Regeneration Using Stem Cells: Strategies and Translational Considerations; by Xin-Yue Xu, Xuan Li, Jia Wang, Xiao-Tao He, Hai-Hua Sun, Fa-Ming Chen

THREE DIMENSIONAL PRINTING

The inkjet model uses inkjet printing with liquid and powder solutions to produce an extracellular matrix, select and eliminate cells, and use a tailored scaffold [31]. A 3D fibre scaffold was used by Park et al. (2012, 2014) to direct PDL cells and promote tissue calcification. The use of a 3D scaffold in socket preservation with normal bone healing and better-preserved volume was examined by Goh et al. (2015)[1].

Fusion model: allows for the construction of customised scaffolds but excludes the use of cells, growth factors, and proteins [31]. Lactic-co-glycolic acid, a polymer with good resorption and mechanical strength properties, is the substance employed.

The creation of a soft hydrogel scaffold with facile cell integration using 3D plotting is possible. Possible suppression of cell-to-cell communication, which affects the signalling and proliferation process, is a drawback [32,33]. On the other hand, using living cells in the scaffold produces excellent tissue creation outcomes .[1]

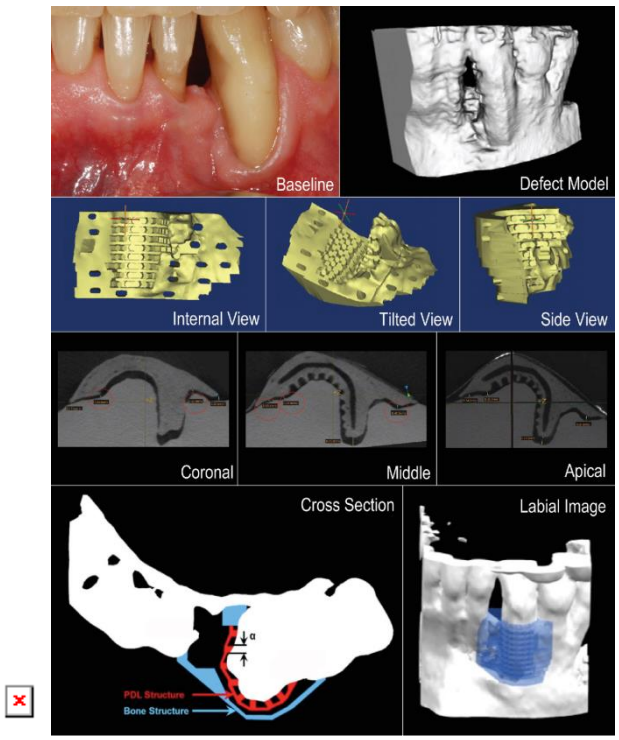

Fig 21:3D-printed Bioresorbable Scaffold for Periodontal Repair; G. Rasperini, S. Pilipchuk, C. Flanagan, C.H. Park, G. Pagni, S. Hollister, W. Giannobile

Conclusion: Many regenerative therapies are used to replace the lost periodontium tissues, and biomaterials are crucial to these treatments. From a tissue perspective, the regeneration around implants appears to be simpler because only bone is being replaced, but it is still a crucial area because it lacks blood arteries, vital growth hormones, and proteins like those in a tooth. In order to have a reliable regeneration, many factors must be taken into account. These factors include managing the occlusal load, taking into account the biomaterial's mechanical stability and improvising accordingly, the decreased FBR due to chemical and thermic treatments that allow the processing of particles, the microbiological flora around the defects, controlling dysbiosis, and, lastly, wound stability.

It's important to consider the chance that the grafts could become exposed to an infection and fail. With the existing therapeutic choices, partial regeneration of the periodontal tissue is now feasible; nevertheless, functional regeneration of significant abnormalities brought on by severe periodontal disease is still not conceivable. For the successful reconstruction of periodontal tissue, it is crucial to better understand the cellular and molecular mechanisms underlying periodontal development and, consequently, to identify the suitable functional molecules that induce the differentiation of stem cells into periodontal lineage cells.

The discipline of periodontal bioengineering has entered a dynamic new stage of development that will significantly benefit the patient. A real "coming of age" for the area may be seen in the vigorous

exploration of various biological technologies for clinical translation. However, adequate delivery methods, immunogenicity, the distinction between autologous and allogenic cells, the identification of tissues that give the most suitable donor source, control of the entire procedure, and cost-effectiveness are all significant factors that should not be ignored. The use of technology will surely advance periodontal bioengineering. Innovations in biomaterials engineering will be crucial for creating new applications and enhancing existing ones. Stem cell-based regeneration will only develop as a result of advancements in stem cell biology. Improved knowledge of the molecular processes through which substrate interactions affect and vary stem-cell self-renewal.

The beginning is crucial for the targeted design of biomaterials. Developmental biology and functional genomics advancements should also be taken advantage of to increase the range of biological molecules that can be included into biomaterials to fine-tune stem cell functions. With the merger of the two potent fields of stem cell biology and biomaterials engineering, we now have a fresh blank canvas on which to create treatments that have the potential to transform periodontal tissue engineering.

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