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Review Article

Tissue Engineering in Dentistry- Boom in Dentistry

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***ABSTRACT*:**
Tissue engineering is a novel as well as highly exciting field of the research. It may be possible with the techniques of tissue engineering to repair the damaged tissues or even to create the replacement organs. The present article reviews the typical key elements, principles underlying the key tissue engineering strategies and its implication in dentistry. The examples of tissue engineering include the passive approaches like dental implants, as well as the inductive approaches where the specific molecular signals are used to activate the cells.
Key words: Tissue engineering, tissue induction, cell transplantation, gene therapy.

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INTRODUCTION:
The term "*tissue engineering*" was coined in 1987 at a National Science Foundation (N.S.F.) bioengineering meeting in Washington D.C. The branch of tissue engineering follows the principles of material science, cell transplantation and bioengineering towards the development of the substitutes that would restore as well as maintain the normal function.[1] In 1988, Shalak & Fox defined tissue engineering as "the application of principles & methods of engineering & life sciences, to obtain a fundamental understanding of structural & functional relationships in novel & pathological mammalian tissues, & the development of biological substitutes to restore, maintain or improve tissue function". The fundamental of tissue engineering builds upon the interface between the material science, biocompatibility, cell integration, natural or synthetic scaffolds and also specific signals in order to create the new tissues. Historically, some of the earliest attempts at tissue replacement, dating back to the thousands of years, have involved the teeth.[1]In today's modern times, dentistry continues to emphasis on and also be a leader in the study as well as the use of biocompatible materials. In current times, the replacement of lost or

deficient tissues involves the use of the prosthetic materials, medicinal therapies as well as tissue and organ transplantation. However, all of these have limitations; such as inability of synthetic prostheses to replace any but the simplest structural functions of a tissue.[2] These problems have driven the development of tissue engineering, which can be defined as a 'combination of the principles and methods of the life sciences with those of engineering in order to develop the methods and materials to repair the diseased or damaged tissues and also in order to create the entire tissue replacements.[2] Tissue engineering holds a promise of producing better organs for transplant. By using the techniques of tissue engineering as well as gene therapy, it may be possible to correct many genetic defects which otherwise are incurable. [3]A major objective of tissue engineering is the in-vitro construction of the transplantable vital tissue. The artificial tissues can revolutionize the healthcare by providing a supply of soft as well as hard tissue on demand. The aim of this brief review is to light upon the need of tissue engineering, its key elements, various strategies and implication in dentistry with a general perspective and also background on the tissue engineering, moreover an overview of what has been accomplished in this field so far, and thereby consideration of the impacts of tissue engineering on the practice of dentistry over the next 25 years.

KEY ELEMENTS OF TISSUE ENGINEERING:

The key elements of tissue engineering are stem cells, morphogens, scaffolds and bioreactor. Tissue engineering is basically the branch which is based upon the synchronization of these key elements. [4]

Stem cells- The stem cells are defined as unspecialized cells which are capable of both the self-renewals for long periods and also multi-lineage differentiation, which contribute to regenerate the specific tissues. Hence in order to restore the damaged tissue or organs, it is very crucial to understand the fundamental developmental process behind the regenerative medicine and tissue engineering. [5]The stem cells play essential roles in the field of tissue engineering for tissue repair as well as organ development. The two main types of stem cells that have been studied are embryonic stem cells (ES cells) and adult or postnatal stem cells (AS cells). The oral stem cells mainly include: Stem cells from exfoliated deciduous teeth (SHED), Dental pulp stem cells (DPSCs), Stem cells from apical papilla (SCAP), Periodontal ligament stem cells (PDLSCs), Mesenchymal stem cells from gingiva (GMSCs), Progenitor cells from oral mucosal lamina propria (OMLP-PCs)

Morphogens- The morphogens are proteins that induce the cell signaling which influence the critical functions like matrix synthesis, cell division and proliferation. They are basically extracellularly secreted signals which govern the morphogenesis during the epithelial-mesenchymal interactions. Some of the morphogens are Transforming growth factors beta-1, Fibroblast growth factor 2 & 9, Bone morphogenic protein and Vascular endothelial growth factors. [6]

Scaffolds- Scaffolds are the materials that have been engineered in order to cause the desirable cellular interactions for contributing to the formation of new functional tissues for various medical purposes. [7]The scaffold provides a physicochemical as well as biological 3-D microenvironment for the cellular adhesion, migration, growth and differentiation. It basically acts as a carrier for morphogens in the cell therapy.

Bioreactor- Term "bioreactor" refers to a system in which the conditions which are closely controlled in order to induce or permit certain behavior in the living cells or tissues.[6, 7] The primary aim and objectives of these systems are to establish the spatially uniform cell distributions on the three dimensional scaffolds, to maintain the desired concentrations of gases and the nutrients in culture medium, and also to expose the developing tissue to the appropriate physical stimuli.[7]

STRATEGIES OF TISSUE ENGINEERING- The strategies employed in order to engineer the tissues can be categorized into three major classes: Cell conduction therapy, Cell induction therapy and cell transplantation. These strategies depend upon the use of one or more key elements for example cells, growth factors and matrix to guide tissue regeneration.

A. Conductive approach makes the use of a barrier membrane in order to exclude the connective tissue cells that will interfere with regenerative process and thereby enabling the desired host cells to populate at the regeneration site.

B. Inductive approach uses a biodegradable polymer scaffold as a vehicle in order to deliver the genes and growth factors to the host site. Genes or growth factors can be released at a controlled rate.

C. Cell transplantation strategy uses a similar vehicle for the delivery in order to transplant the cells and partial tissues to host site.

APPLICATION IN DENTISTRY: The engineered tissues will find many applications in dentistry within the next few years. Some of them are listed as follows:

A. Dentin-pulp complex- The stimulation of differentiation of the pulp progenitor cells into the

odontoblast-like cells or secretion of TGF which plays a key role in the recruitment of progenitor cells, cell differentiation, angiogenesis and finally the mineralization of injured area. Stem cell therapy has been attempted for the regeneration of dentine-pulp complex. The dental tissues are a very rich source of the stem cells.[8]

B. Periodontium- Recent advance in the field of tissue engineering utilizes the growth factors as well as cytokines for the periodontal regeneration. [8, 9] The guided tissue or bone regeneration membrane (GTR/GBR) utilizes the occlusive membranes in order to maintain the defective space and selectively encourage the appropriate cells to regenerate the lost tissues and also support the newly formed tissues. [8, 9]

C. Bioengineered teeth- Odontogenesis or the tooth development is a complex process which involves a series of reciprocal epithelial–mesenchymal interactions and the coordination between crown and the root with its associated periodontium. Accordingly the cells get dissociated from the epithelium as well as mesenchymal tissues of the prenatal or postnatal tooth germ were used in order to reconstitute a ‘‘bioengineered tooth germ’’ in vitro. The transplantation of bioengineered tooth germ into the oral environment or an organ culture has been then attempted to produce a whole tooth.[9]

D. Skin, oral mucosa, facial muscles and salivary glands- The tissue engineering has made an extensive progress in the area of skin regeneration and in recent time several skin substitute products (epidermal, dermal or composite) are now available commercially. Keratinocytes sheet has been used which has the ability for the renewal throughout the patient’s lifetime and also can undergo the differentiation and organization after grafting.[8, 9] Development of the engineered oral mucosa also followed the same protocol i.e., started with development of the epithelial sheet. Recently, for skin or mucosal grafting procedures, the plastic compressed collagen has been extensively investigated as a potential scaffold. The facial muscles have a unique anatomy and fibre composition compared to that of other skeletal muscles. The tissue engineering thereby holds a strong promise for the future treatment of the patients with partial tongue resection and facial paralysis.[9] The key issue for the clinical application of tissue engineered muscle is finding a 3- D scaffold that fulfils the demands of the elasticity, biocompatibility and stability. The tissue engineering provides a biological substitute for the impaired salivary glands. However, the main challenge is to culture the cells of human salivary gland as they are highly differentiated and are difficult to expand in vitro.

E. Temporomandibular joints and Bone – The application of autogenic periosteal cells-seeded polymer fleeces to augment the floor of the maxillary sinus before the implants insertion showed the encouraging results from both the radiographical as well as the histological examinations.[8, 9] For irregular defects, the injectable composites can be useful for the stem cell-based bone engineering. The temporomandibular joint (TMJ) is one of the most difficult tissues to treat because of the limited blood supply and thereby the limited capacity for self-repair. In order to regenerate this unique articular cartilage, cell therapy comes first and also the injectable smart hydrogels could be employed for transferring the cells.[9, 10]

FUTURE OUTLOOK- A new era of therapeutic medicine has been provided by tissue engineering; it is rapidly progressing and also extends in order to involve all the tissues in our body. Tissue engineering was an idea three decades ago and today it has become a potential therapy for several conditions.[10] In order to have more regenerative breakthrough for developing and leading to off-the-shelf bio-products to replace a variety of lost tissues and organs, a thorough understanding of embryonic development and also stem cell biology are required. Regenerating particularly the oral tissues is very challenging and also requires recapitulation of the biological development of several tissues and interfaces.[9, 10]

CONCLUSION: The dental practice has always been affected by the new technologies, whether it is the development of the modern restorative materials, high-speed handpieces or tissue engineering. Tissue engineering brings the power of modern biological, physical and chemical science to solve the real clinical problems. Thereby this should yield numerous clinical benefits in dentistry such as enhanced maxillary and mandibular grafting procedures,improved treatment for intraosseus periodontal defects; and possibly even allowing lost teeth to be re-grown; moreover, use of devices such as an artificial salivary gland and muscle (tongue) or mucosal grafts to replace the tissues lost through the trauma or surgery.

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