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Mother Touch in Periodontal Therapy: Chorion Membrane

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Abstract:- Periodontal regeneration is an old idea that is evolving because to the adoption of more modern and altered barrier membranes to get better clinical results. The placental amnion and chorion membranes are examples of these membranes. Its biocompatibility and capacity to speed up wound healing led to its initial use.As part of guided tissue regeneration and guided bone regeneration, the membrane has been utilised in periodontology to reduce probing pocket depth, raise clinical attachment levels, and encourage bone formation. Since these membranes are biologic, they can be broken down by the body and work with tissue.It has also been utilised to treat intrabony abnormalities, guided bone regeneration, and root covering therapies. The special characteristics of this membrane that make it ideal for periodontal surgery, together with the clinical repercussions and literature evaluation.

Keywords:- *Periodontitis, Periodontal Therapy, Biologic Membrane, Chorion Membrane, Periodontal Regeneration.*

I. INTRODUCTION

Periodontitis is an inflammatory disease of the supporting tissues of the teeth produced by individual germs or groups of microbes that causes progressive destruction of the periodontal ligament and alveolar bone, resulting in periodontal pockets, gingival recession, or both.[1] Periodontal therapy can restore inflamed gingiva to near-normal condition. Surgical and non-surgical treatment options are available based on the severity of the periodontal disease. In cases of severe periodontitis and a few cases of intermediate periodontitis that do not respond to non-surgical treatment, surgical intervention is used. Periodontal therapy's primary purpose is to repair, regenerate, or restore damaged tissues.[2]Regeneration is the process through which the body's architecture is naturally renewed through the proliferation and differentiation of newly formed cells and intercellular molecules. The repair only replaces the original. The restoration simply replaces the wounded root surface's natural sulcus at the same level as the periodontal pocket. Because the periodontal apparatus is produced by regeneration via selective cell repopulation, it is desirable to repair it.[1]

The amnion, the innermost of the two human foetal membranes, comes into contact with the amniotic fluid, the foetus, and the umbilical cord as well as other components of the amniotic sac. The amnion is separated from the decidua and the maternal uterus by the chorionic membrane, which is joined to the exterior of the amniotic membrane.[3-4]

Throughout pregnancy, amniotic fluid, which is contained in the sac created by the foetal membranes, surrounds the human foetus. It's crucial to remember that the chorion and amnion are both entirely composed of foetal tissue. It is very likely that some amniotic fluid is transferred directly from the foetus through its membranes to the uterus or placenta. A relatively recent development in dentistry, placenta allografts saw the release of their first commercial product in 2008. The distinct inherent biologic properties of placenta allografts facilitate wound healing and may spread regeneration.

II. HISTORICAL BACKGROUND

For almost 70 years, human foetal membranes have been employed successfully in a variety of applications. In 1910, Davis reported the first use of foetal membrane in skin transplantation.Stern described the use of human foetal membrane to restore wounded and ulcerated skin surfaces in 1913.5De Rith was the first to report on the usage of foetal membranes in the ocular surface in 1940. He treated conjunctival diseases with fresh aminion and chorion as a biological dressing material. Kim and Tseng (1995) identified the most effective method for retaining the biologic features of membranes. The prominence of the foetal membrane has been attributed to a number of causes. For starters, it lowers scarring and inflammation while also speeding up wound healing. Second, its antibacterial properties function as scaffold for cell proliferation and differentiation. Third, the extracellular matrix and its components, such as growth factors, imply that it is a biomaterial that is well-suited for use as a native scaffold in tissue engineering. Finally, it is simple to obtain, process, and transport.

III. THE STRUCTURE OF THE CHORION

The amnion on the inside and the maternal decidua on the outside are in contact with the chorion, the outermost of the two foetal membranes. While "outer" refers to the area or layer closest to the myometrium, "inner" refers to the region or layer closest to the amniotic cavity. The placenta is made of chorion, which is composed of hypertrophied chorion frondosum villi. In histological sections, the

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chorionic villi that run the length of the chorion (chorion laeve) atrophy and appear as obliterated or ghost villi. There are four stages in the non-placental chorion. These originate from within:

- Cellular Layer
- Reticular Layer
- Pseudo-basement Membrane
- Trophoblast

- *Cellular layer*

A thin layer made up of an interlacing network of fibroblasts. When assessed at term, it is commonly defective or totally absent from the chorion. It is, however, simpler to detect in the early stages of pregnancy.

- *Reticular Layer*

This makes up the vast majority of the chorion's thickness and is made up of a reticular network with parallel fibres. Collagens I, III, IV, V, and VI make form the reticular network. Nodes can be found on the branching of the fibres. There are a few fibroblasts and Hofbauer cells (single nucleated macrophages).

- *Pseudo-basement Membrane*

This is the trophoblast's foundation membrane. It is a dense layer of argyrophil connective tissue that connects to the reticular layer above and sends anchoring and branching fibres down into the trophoblast. The basement membrane uses collagen IV, fibronectin, and laminin to connect the trophoblasts to the reticular layer.

- *Trophoblast*

The chorion's deepest layer is made up of 2 to 10 layers of trophoblast cells that are in contact with maternal decidua on their deeper side. This stratum contains destroyed chorionic villi.

IV. COMPOSITION OF HUMAN CHORION MEMBRANE:

Fibronectin, laminins, and collagen types I, III, IV, V, and VI are extracellular matrix (ECM) proteins present in chorion. These ECM proteins are essential for chorion tissue biocompatibility5. Collagen is highly tolerated and bioabsorbable, has hemostatic properties, and encourages autogenous connective tissue (CT) migration close to it. Fibronectin is involved in many biological processes, including tissue healing, blood coagulation, cell migration, and adhesion."" also includes platelet-derived growth factor AA (PDGF-AA), transforming growth factor B (TGF-B), keratinocyte growth factor (KGF), vascular endothelial growth factor (VEGF), and basic fibroblast growth factor (b-FGF), as well as interleukin (IL)-4, 6, 8, and 10, and tissue inhibitor of metalloproteinase 1 and 2. (TIMP 1 and 2) which promote periodontal regeneration, [6-7]

- *Properties of membrane:*

Professor VP Filatov, a Russian ophthalmologist, outlined the synthesis of placental extract in the Principle of Therapeutic Tissue. Prior to Filatov's inquiry, despite the fact that it had been used for over a century in Europe and portions of Asia, most notably China, Korea, and Japan, there was no record of its therapeutic usefulness. There was an increase in research on human placental extract after his description. Filatov began researching human cornea grafting using the theory of preserved material transplantation. He established that when animal or vegetable tissues are detached from the organism and subjected to external environments, they undergo a metabolic readjustment. elements that impede their critical functions. As a result, the tissues start producing substances that encourage critical functions. Filatov,[8-9]named these substances "biogenic." stimulators.

Human chorion membrane is a biological graft with distinct biologic properties that can reduce inflammation, eliminate adhesions and scarring, control angiogenesis, and improve wound healing [10-11]. Chorion membrane promotes epithelialization, maintains appropriate epithelial phenotypes, and possesses antimicrobial capabilities.

- *Anti scarring property*

Fibroblasts are naturally responsible for scar formation during wound healing, and they are driven by transforming growth factor, which is secreted in the wound area by macrophages and fibroblasts,[12]

- *Chorion membrane Promotion of epithelialization*

The chorion membrane Chorion membrane supports epithelial cell mobility, basal cell adhesion, epithelial differentiation, epithelial apoptosis, and epithelialization during wound healing.Growth factors produced by the chorion membrane, such as keratinocyte growth factor, basic fibroblast growth factor, and transforming growth factor B, can promote epithelialization. Because of its high concentration of laminin-5, mitogenic growth factors, and anti-inflammatory proteins, chorion membrane promotes epithelial cell proliferation, migration, adhesion, and differentiation. Because laminin has a high affinity for binding epithelial cells,[13] unlike prior reported membranes, this barrier enables for rapid epithelial cell expansion rather than exclusion." Its basement membrane provides a secure and appropriate environment for the growth of epithelial cells. When compared to other synthetics, its high permeability enables. In comparison to other synthetics, its high permeability enables for optimal oxygenation of epithelial cells: (HGF) that reduces scarring by maintaining a proper TGF-1 and TGF-3 equilibrium. [14-15] It also reduces the risk of fibrosis by reducing fibroblasts' expression of transforming growth factor and its receptor. As a result, the chorion membrane regulates wound healing by encouraging tissue regeneration over scar formation. Fibronectin also inhibits myofibroblast differentiation.

- *Anti-inflammatory property*

It is hypothesised that the membrane, by functioning as a barrier, prevents the influx of inflammatory cells and, as a result, inflammatory mediators to the wound area. In the chorion membrane, mesenchymal stem cells (MSCs) inhibit a variety of immune cell inhibitors, including secretory leukocyte proteinase inhibitor and elafin. [16-17] Many inhibitors have antibacterial properties in addition to anti-

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inflammatory properties.They function as innate immune system components, protecting related surfaces against infection.

➢ *Lack of immunogenicity*

The chorion membrane, which is made up of trophoblast cells, has a distinct molecular surface architecture and biochemical properties that make it immune to maternal immune attack. HLA-G expression appears to be the most critical factor in preventing trophoblast rejection. Non-polymorphic class I molecules, including HLA-G, are expressed in extra-villous cytotrophoblast as well as amnion cells and amniotic fluid, in contrast to HLA-A and B class I genes, which are down regulated in human trophoblast cells. The highly polymorphic classical class I molecules HLA-A, B, and C are responsible for generating a specific immune response by presenting peptide antigens to T cells. HLA-G, on the other hand, is thought to have a role in the induction of immunological tolerance by acting as a receptor. Because the chorion membrane is derived from foetal tissue, all of the preceding qualities apply.

Chorion cells do not exhibit HLA-A, -B, -D, or -DR antigens on their cell surfaces, but they do express HLA-G, implying that severe rejection would not occur following transplantation.[18-20]These mesenchymal stem cells vary from other nucleated mammalian cells in that they exhibit limited allogenic response when supplied to MHC mismatched adult immunological competent recipients. [21] Membrane also has immunomodulatory effects on CD86 and CD40 in the presence or absence of Interferon-Y (IFN-Y). Furthermore, because they lack the expression of co-stimulatory cell surface molecules like CD80, they actively reduce T cell, dendritic cell, and B cell function, which inhibits excessive inflammation. Although the immunogenicity of the foetal membrane is debatable, it is widely assumed that it is not immunogenic. Furthermore, it is widely assumed that cryopreserved foetal membrane tissue has lower immunogenicity than fresh foetal membrane tissue and that cryopreserved cells are nonviable. Tissue grafts made of placental membrane components are deemed to have "immune privilege" since they pose a minimal risk of immunological rejection. [22-23]

➢ *Antimicrobial and Antiviral Properties*

Because of its antibacterial and antiviral capabilities, foetal membrane reduces the risk of infection.[24] Kjaergaard et al[25] 2001 shown that the amnion and chorion exhibit antibacterial properties in vitro against specific pathogens. The presence of cystatin E, an analogue of cysteine proteinase inhibitor, contributes to its antiviral activities. Chorion membrane (CM) has a strong antibacterial impact because it produces human beta-defensins (hBD) and forms an early physiologic "seal" with the host tissue, acting as a physical barrier against the external environment. The membrane binds securely to the wound via fibrin and elastin connections, sealing the wound and preventing infection. This strong adherence aids in the restoration of lymphatic integrity, protects circulating phagocytes from exposure, and allows for the faster elimination of pathogens. [10] Furthermore, the hemostatic feature of chorion basement membrane collagen fibres prevents hematoma formation in clean surgical wounds. This minimises bacterial burden and illness risk by preventing germ buildup. In addition, the chorion membrane expresses two low-molecular-mass elastase inhibitors, secretory leukocyte proteinase inhibitor (SLPI) and elafin." Elafin and SLPI, in addition to their anti-inflammatory activities, contain antibacterial capabilities and operate as components of the innate immune system to protect associated surfaces against infection. [17]

The antimicrobial activity of MSCs in the foetal membrane is achieved by two mechanisms: directly through the secretion of antimicrobial factors such as LL-372, and indirectly by the production of immunomodulatory factors that upregulate bacterial death and phagocytosis by immune cells.[27]

➢ *Cell Differentiation Property*

Foetal placental tissues have the ability to differentiate into various cell lineages. The hematopoietic lineage can be found in the chorion, allantois, and yolk sac, whereas the mesenchymal lineage can be found in the chorion and amnion. Because they have these features, cells isolated from the chorion are good sources of hematopoietic and mesenchymal lineages.[28]

The human placenta's foetal membranes contain stromal/mesenchymal tissue at the point of contact between the trophoblastic area of the chorion and the amniotic epithelial layer. Bailo et al. (2004) identified amniotic and chorionic membrane mesenchymal stem cells (MSCs). The absence of haematological and endothelial markers, as well as the expression of CD29, CD44, CD73, CD105, and CD166, are widely accepted phenotypic hallmarks of placenta-derived mesenchymal cells.22CMCs can differentiate into the osteocytic, chondrocytic, and adipocytic mesodermal lineages, showing the existence of mesenchymal progenitors. Interestingly, placenta-derived mesenchymal cells can also generate neuron-like cells, implying that this tissue contains cells capable of undergoing both mesodermal and ectodermal lineage development. Foetal mesenchymal placental cells have the following morphological characteristics:The morphological features of fetal mesenchymal placental cells include plastic adherence and fibroblast-like growth. Portmann-Lanz et al. (2006) have reported that cells from amniotic and chorionic mesenchyme undergo cell death after four or five passages, CD271 can be used as marker in placenta-derived mesenchymal cells to isolate populations with high clonogenic and osteogenic potential,[29]

Plastic adhesion and fibroblast-like development are two morphological characteristics of foetal mesenchymal placental cells. Cells from amniotic and chorionic mesenchyme die after four or five passes, according to Portmann-Lanz et al. (2006), and CD271 can be utilised as a marker in placenta-derived mesenchymal cells to identify populations with significant clonogenic and osteogenic potential,[29]

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Additionally, chorion membrane-derived MSCs (CM-MSCs) suppress allogeneic immunological responses. MSCs modulate immune function primarily through soluble substances such as transforming growth factor beta (TGF-B), 250 hepatocyte growth factor (HGF), [30] prostaglandin E2 (PGE), and 31 indoleamine 2, 3 dioxygenases (IDO). These substances released by placenta-derived MSCs may decrease immune cell proliferation and inflammatory cytokine production: [25-32]Furthermore, cell-cell interaction is a putative mechanism influencing immunological regulation. [33]Cell-to-cell communication, one of the proposed mechanisms behind MSC immunomodulatory effects is the interaction between MSCs and lymphocytes. Cell-cell interaction between bone marrow-derived MSCs (BM-MSCs) and lymphocytes increased transcription of IL-10 and TGF-B in BM-MSCs. Furthermore, cell adhesion molecules such B7-H1, intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) may play a role in immunological regulation.[24]Human umbilical cord-derived MSCs (hUC- MSCs) modulate immunity mostly through cell-cell interaction via adhesion molecules, particularly B7-H1[34]

➢ *Accelerated wound healing*

Inflammation, proliferation, and remodelling are three overlapping stages in the complex biological process of normal wound healing. 35Neovascularization, stromal deposition, and epithelialization are the results of this process, which involves the coordinated interaction of several cell types, is fueled by extracellular matrix interactions, and cytokine production. Mesenchymal stromal cells (MSCs) and hematopoietic progenitor cells (HPCs) have been proven to aid in wound healing. creating paracrine factors that stimulate angiogenesis, extracellular matrix formation, and tissue regeneration while promoting cell migration and proliferation. As a result, these cell types have drawn a lot of attention for use in applications related to wound healing [37-38]

Two broad strategies for therapeutic application of stem cells in chronic wounds are
(1) direct introduction of autologous or cryopreserved allogeneic stem cells to the wound and
(2) recruiting endogenous stem cells to the wound and increasing their wound healing capability are two major techniques for therapeutic application of stem cells in chronic wounds.

The human chorion membrane is in charge of attracting endogenous progenitor cells to the wound. It contains a number of growth factors and cytokines and has been found to increase fibroblast and endothelial cell proliferation as well as the recruitment of MSCs. encourage the expression of growth factors in native cells and stimulate peri matrix neovascularization, while their structural component serves as a scaffold for tissue regeneration 1[4] MSCs have also been shown to control immunological and inflammatory responses during wound healing. These progenitor cells often decrease pro-inflammatory cytokine secretion, such as tumour necrosis factor-a and interferon-y, while increasing anti-inflammatory cytokine production, such as IL-4 and IL-10, [39-40].The anti-inflammatory capabilities of chorion membrane may be due to the synergistic effects of both the scaffold's inherent anti-inflammatory cytokines and the scaffold itself. The consequences of recruited progenitors.[41]

The nature of the biocompatibility and healing capacity of the chorion membrane may be linked in part to the presence of growth factors and TIMP-1 in the chorion basement membrane.4 Laminin is a glycoprotein heterotrimer that consists of an a-chain, a B-chain, and a y-chain. There are five types of a-chains, three types of B-chains, and three varieties of y-chains. At least 15 different types of laminin result from different combinations of these chains.42 Laminin-5 promotes cell adherence on the cell membrane's surface via integrin-mediated attachment. This property of lammin-5 is most likely responsible for gingival tissue's capacity to tightly adhere to membrane and then heal and cling to the enamel surface,"

V. SOURCE OF CHORION TISSUE

Chorion donors must be living mothers who have had a live child by caesarean section or vaginal section. Elective caesarean delivery helps in the choice of a willing donor and the planned collection of chorion membrane because placentas collected after natural vaginal delivery may have structural defects caused by the membrane stretching during labor and delivery and may be infected by normal vaginal flora, herpes, chlamydia, or other contaminant bacteria. Different nations' tissue transplantation regulations require different procedures for preservation, testing, and storage due to the risk of infection with the human immunodeficiency virus (HIV) and hepatitis C. Virus transmission protection is impacted by donor choice and serological testing for known transmissible viruses at the time of donation. three to four months later, this period of time eliminates any potential for infection spread that could be found later.,[20]

A. Processing of Fetal Membrane

For clinical use of the membrane, it can be prepared in the following forms:
1. Fresh membrane
2. Dried membrane
3. Frozen membrane
4. Freeze derived irradiated
5. Cryopreserved membrane

B. Advantages of Chorion Membrane:

1. It offers a different method for enhancing the recruitment and engraftment of endogenous progenitor cells that can hasten wound healing and neovascularization. This eliminates the need for commercially available cryopreserved allogeneic progenitor cells.
2. It does not require special storage or shipping because it is stable at room temperature.
3.It is an angiogenesis-promoting scaffold that draws progenitor cells to wounds.[41]
4. It may work in tandem with recruited cells to reduce inflammation.

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5. Because this allograft self-adheres, there is no need for suturing, making it easier to utilise in posterior lesions.
6. The presence of considerable levels of laminin and laminin-5 across the barrier is crucial due to their strong affinity for binding gingival cells. Epithelial cells may help to improve root surface adaptability.
7. It is a surgical patch that is immunologically compatible and used for a variety of medical purposes.
8. The chorion membrane (CM) functions as a barrier membrane between the gingival epithelium and hard tissue, encouraging periodontal ligament cells to become progenitor cells capable of regenerating new tissues.
9. CM is available in a variety of lengths and widths, allowing for adaptation at the site on both the buccal and lingual aspects of the quadrant in a single strip with interdental trimming.
10. After being placed dry, the barrier quickly becomes hydrated by blood, becoming incredibly pliable and closely mimicking the characteristics of the underlying surface.
11. Carly wound stability is provided by CM when utilised as an internal fixation. Furthermore, it has a thin, self-adherent character.

VI. PLACENTAL MEMBRANE APPLICATIONS BASED ON THEIR QUALITIES INCLUDE VII.

1. The physical properties of foetal membrane have demonstrated that it is compatible with the corneal surface of the eye. Because the immunological modulatory powers of the ocular and placental membranes are so similar, they have been nicknamed "parallel universes" [44]
2. Human foetal membrane is also used as a suitable dressing, with four main goals in mind: haemostasis, water loss reduction through evaporation, providing a moist environment for cell survival and proliferation, acting as a barrier to microbial colonisation, and pain reduction.
3. Foetal membrane is recognised as an important possible source of scaffolding material that must swiftly integrate with host tissue and provide an ex (HSV), varicella zoster virus-infected tissues, and erythema multiforme major.

Dental applications include:
1. Surgical methods for root coverage,"
2. Periodontal pocket treatment with guided tissue regeneration
3. Vestibular augmentation

VIII. LIMITATIONS IX.

1. The use of foetal membranes requires skill; so, operator inexperience is one restriction. [10]
2. The risk of spreading an infection during a transplant of foetal membranes never goes away. It is important to follow particular safety guidelines and precautions when using these biological membranes.
3. Both the procedure and the defect morphology influence how these membranes are used. This method demands expert understanding of periodontal regeneration and wound healing.

X. PERIODONTAL THERAPY WITH CHORION MEMBRANES

Chorion membrane is an immunotolerant semipermeable membrane that can guide tissue regeneration. It fulfils the mechanical GTR concept, which has been expanded to incorporate the biology GTR concept. The biomechanical GTR membrane promotes healing by decreasing surgical scarring and functional loss while simultaneously serving as a food source. Another advantage is that the amniotic membrane is better revascularized. It has the potential to be a fantastic grafting material. It has been shown to improve wound healing, postoperative function, and aesthetics while offering no dangers.[45] In guided bone regeneration, a treatment approach for large bony abnormalities, a barrier membrane is employed to stimulate osteogenesis while inhibiting fibroblast cell multiplication. Lyophilized multi-layered acellular human collagen was used to cure rat tibia deformities in vivo. It acted as a barrier against the invasion and formation of fibrous tissue while also encouraging bone growth.[46]

A barrier membrane is used in directed bone regeneration, a therapy strategy for major bony defects, to induce osteogenesis while suppressing fibroblast cell growth. In vivo, lyophilized multi-layered acellular human collagen was used to treat rat tibia abnormalities. An implant fixture requires 1mm of bone to surround it in dental implant therapy, and the site preservation technique is used to accomplish this. A resorbable amnion chorion membrane was used as a site preservation barrier. Placental allografts have immunoprivileged properties, are antibacterial and antimicrobial, help to reduce wound inflammation, and are permanent.[47]

Amnion chorion membrane, demineralized freeze-dried bone allograft (DFDBA), and xenograft are used to repair intrabony lesions.[48] Improved root coverage, tissue thickness, and gingival tissue connection. Provides excellent cosmetic outcomes while causing little post-operative discomfort or negative effects. Because of its self-adhering nature, processed dehydrated allograft amnion is appropriate for multi teeth operations and recession anomalies. It can be used to treat shallow to moderate Miller's Class I and II recession defects instead of autograft tissue.[45]

The exposed root surface is intended to be hidden through periodontal plastic surgery. Recent research has revealed a resorbable amniotic membrane that supports gingival wound healing and acts as a rich source of stem cells in addition to maintaining the morphological and anatomical structure of regenerated tissues. A relatively recent development in periodontal plastic surgery is this amnion tissue-based allograft.[48]

XI. CONCULSION

Amnion and chorion membranes, for example, offer antibacterial, biocompatible, and antiangiogenic qualities that have made them desirable in the field of periodontal regeneration in recent years. They have long worked in the

medical industry, and they are currently expanding into other branches of dentistry. Their surgical application has a number of benefits. They have drawbacks, just as other inventions. However, they might be changed in the future to increase clinical efficacy.

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