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| 9Dent-2011.weebly.com | Lecture No. |
| 6/12/2015 | Date: |
| Ahmad hamdan | Doctor: |
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Periodontics II

**University of Jordan**

**Faculty of Dentistry**

**5th year (2015-2016)**

Price & Date of printing:

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Principle of guided tissue regeneration

Last time we talked about assessment of periodontal regeneration , define regeneration and repair , and know the types of tissue that are involved in regeneration .

\* Biological foundation for guided tissue regeneration (GTR )

- it will influence what's going to happen

- this's idea come from Compartmentalization (Melcher 1976) >> talked about the differences between periodontal tissue in turnover and the effect that will take place if these tissue left to turnover in healing process .

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| Cell type  | Effect |
| Gingival epithelium (keratenocyte )  | Long junctional epithelium |
| Connective tissue  |  Some degree of root resorption and connective tissue attachment  |
| PDL (mesenchymal cells )  | Cementum and PDL fibers that will be inserted in perpendicular way on the root surface  |
| Alveolar bone  | Ankylosis , bone formation in direct contact with the root surface  |

- the most favorable one and what we need is PDL cells because it's the only effect that mimic the natural tissue .

- to control the regeneration result you have to separate the tissue or to exclude certain tissue from the space where the healing/regeneration take place , by putting membrane (from collagen or other material ) to separate the epithelium and connective tissue from the space inside the bone to allow the mesenchymal stem cell (in PDL and bone ) to enter and occupy the space > so proper wound healing and regeneration achieve .

Same principle if we loss the tooth , we do bone graft for implant , but in this case w called it " guided bone regeneration " .

- membranes :

1) non-restorable membrane : you should reenter and remove it .

2)restorable membranes

- membranes requirements (to use it in cell exclusion) :

1) biocompatibility

2) cell exclusion : when you put membrane you prevent the epithelium cell and connective tissue (fibroblast) to migrate to the defect area and occupy it , so you give the bone cells and mesenchymal cells in PDL enough time to occupy the defect area ) .

 \*mesenchymal cells need longer time than CT and epithelium cells

3) space maintains : provide us the capacity to maintain the space during the whole process of healing

4) tissue integration : no immunologic reaction

5)easy of use and handling

6) biological activity

Non resorbable membrane : more than one type the most using one is expanded polytetrafluroethylene (ePTFE ), another types millipore membrane and rubber dam membrane (theoretically , use in animal studies , have problem with tissue integration ).

EPTFE : tissue integration not very good , but it's one of the best materials on the market know .

-to be able to use non-resorbable membrane you must have :

1)sufficient one or zone of keratinized area .

2) the surgical flap which i will put it on the membrane must have enough thickness .

- if the membrane don't have good tissue integration , tissue may go far away from it !

So i need keratinized and thick tissue to resist better > prevent exposure of membrane > which if happen lead to inflammation and bacteria accumulation > infection > failure of the procedure especially if it' happen in the early stage of healing after surgery .

- also another point for needing it to be thick ; to be easy to handle When we want to open it again and remove it ( remember we talk about non-resorbable membrane ) .

In non-resorbable membrane healing is allowed for 4-6 weeks at least , ideally 12 weeks but it's not easy to maintain the membrane in it's place for 12 weeks !

No probing should be perform in the early stage , the first 3-6 months , ideally it should be 9 months to establish integration and maturation of PDL fibers .

Radiograph evidence of bone formation will be observable after 12 months .

Also in addition to enough keratinized tissue and thick flap , we must have excellent oral hygiene , otherwise perforation happen infection will occur and procedure fail .

- Bio - resorbable membranes :

1) polyglycoside synthetic membranes PGA/PLGA : the problem with is is biodegradation or resorption which is fast and associated with certain degree with inflammation !

So the result not good comparing to classical one (collagen )

2) collagen : type I or type I+III , from porcine (peg) or bovine (cow )

The most using one type one+three

Type III cross link to collagen type I , so as we increase collagen type III resistant and rigidity will increase and the rate of resorption will decrease and rhe migration will be difficult .

3) calcium sulfate

- the bio-resorbable membrane easier to handle than non-resorbable one :

1) more tissue compatible

2) time of resorption can be regulate

3) second surgery for membrane removal is not required

Bio-resorbable membrane lack rigidity which is the main disadvantage ; if the area i want to make regeneration on it is one wall defect, it will be more difficult to maintain using resorbable membrane ;because collapse will happen so i must use bone under it .

On other hand i can use non-resorbable membrane especially if NiTi bar used , by using it the epithelium wight can't push the membrane downward .

\* the result

 - the main probing attachment gain was about 4 mm along with reduction of probing pocket depth up to 6mm

- bone fill was 4.3mm

- GTR before surgery probing attachment level is 11mm , after a year 5.6mm

-probing pocket depth was 7.9 mm , after surgery become 2mm .

- Guided tissue regeneration in intrabony defect

Reselute (brand name for resorbable membrane ) VS. core-TEX (ePTFE , non-resorbable )

- equal reduction of pocket depth

- recession approximately the same

- statistically no difference, so regarding the clinical performance no different between the both .

- class II furcation defect

- buccal to lower first molar

-no statistical difference , the are comparable

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| Membrane category  | Advantages  | Disadvantages  |
| Non-resorbable | - numerous studies demonstrate their success - may be titanium reinforced - remain intact until removal-easily attached with titanium or resorbable tacks- greater bone fill if membrane not exposed - minimal tissue response if membrane not exposed  | -require a second surgery for removal - increase patient morbidity - if exposed , must be removed - can be technique sensitive  |
| Resorbable | - numerous studies demonstrate their success - does not require surgical remove - decrease patient morbidity - improved soft tissue healing - tissue friendly reaction to membrane exposure - cost effective , one surgery only - does not have to be removed if exposed  | -uncertain duration of barrier membrane function - difficult to tack down - slightly less bone fill than non resorbable membranes - inflammatory response from tissue may interfere with healing and GBR (Guided bone regeneration) - can be technique sensitive  |

\* membrane +/- bone graft

- specifically we talked about defect related to teeth

- classII furcation involvement , buccal to lower molar > is the most predictable type of defect to be regenerated by bone graft .

- the maxilla non predictable

- this is periodontist opinion , on other hand surgeon opinion is different : talked bout edentouls and major , take large graft and put it , theses true according to the blood supply , morphology and geometry of bone is different ; cortical bone in the mandible more than maxilla so less blood supply and less predictable bone regeneration outcome .

Perio > the mandible more predictable.

Surgeon > the maxilla more predictable

- in general if teeth present defect around it more predictable in the mandible .

- GTR with DFDBA ( demineralized freeze dried bone allograft ) the critical attachment level (CAL) gain is 2.27

GTR alone 3.11

So no different between the two groups

After 12 months there's a slight different, about 1 mm more in GTR alone !

But we must notice that the defect was not exactly the same .

- Generally speaking, with or without bone graft below the membrane , the result could be the same , depending on the anatomy .

This is true if the defect was comparable, but if there is extensive bone loss it's mandatory to put bone graft .

New approaches to periodontal regeneration

- what we described before were classical approaches (GTR , bone graft , ... )

- now we will talked about recent one

-for large defect ( for example i have only the floor ) , which is not enough to give me blood supply and stem cell i can use these approaches , which include :

1- Enamel matrix derivative (EMD) : protein influence the formation of enamel during the development , also have a role in PDL regeneration

2- growth factors

3- platelet rich plasma (PRP)

4- bone morphogenetic proteins (BMPS)

5- gene therapy

6- tissue engineering

\* the most important one is **enamel matrix derivative** , the most used one in Europe , many literature done on it .

- induction of cementogenesis

- come from Hertwig's epithelium root sheath .

- the one which is found in the market is porcine origin

- amelogeneins + ameloblastin + enamelin + polyglycolic acid (PGA)

- PGA : work as vehicle that protect the protein

 - the capacity to precipitates to the root surface ; when you add it will adhere to the root surface .

How we use it ?!

- root conditioning with prefGel

- application of Emdogain (brand name )

- precipitation of amelogenins on root surface (matrix formation)

- clot formation

- granulation tissue (normal healing process )

- migration and adhesion of mesnchymal cell (MSCs)

- Proliferation of MSCs

- cytokine production

- Proliferation and differentiation of MSCs on the root surface

- differentiation into cementoblasts

- deposition of cementum

- insertion of periodontal ligament fibers into newly formed cementum

- filling of defect with newly formed periodontal tissues

- parallel formation of alveolar bone in the defect

- finally we would obtained periodontal regeneration with a new functional attachment and new functional alveolar bone .

Someone ask if we always obtained these results ?! Clinically the result almost always obtained in animal study , in human many case yes but you will not obtain the same result in all area around the tooth , you will obtained it in the deepest part ( the nearest one to blood supply and stem cells ) .

When you go up the defect will be larger and have some difficulties , you will have some formation of long junctional epithelium and ankylosis .

* So in enamel matrix derivative we will have :

Regeneration of cementum

Bone formation

PDL formation

No recession

No junctional epithelium

\* **growth factors**

- there are many growth factors

- theoretically speak , if we apply a certain growth factor at certain time it will help in regeneration , how ? For ex. Platelet derived growth factor will increase chemotaxis , cell proliferation and matrix gene expression .

- this study made in vitro

- but we don't know if we add another growth factor like transforming growth factor beta what will happen !

- in bone cell , platelet derived growth factor (PDGF ) and transforming growth factor > there will be proliferation but there's no differentiation , we must remove PDGF to allow differentiation to happen , but we don't know when to remove , what's the concentration , what's other cell we need and many other things .!

Much more difficult process than what appear or what some company show to us .

 But now we cane use culture with different cell and membrane to study it .

- these growth factors may be found in separate form or combined form like PDGF .

- there's net different between using PDGF and open flap and debridement alone , of course the result with PDGF will be better .

- the problem with growth factors is we don't know about there complication , so deal with them with caution .

- platelet rich plasma ,available as membrane (from fiber ) or gel form , but there is no established result that it will help in regeneration of tissue until know

- factor effect GTR in deep intrabony defect ( influence predictability of regeneration not the success of procedure):

1) width/ depth of defect as the depth increase it will be better , deep and narrow better than wide and shallow defect

Narrow > 3D volume between tooth and bone less

Deep > large area with bone walls that can give me blood supply

2) morphology of defect ( number of defect wall )

3) good oral hygiene ( infection control )

4) coverage by membrane

5) coverage of new tissue

- when we move from right to left it will be better

Vertical defect better than horizontal

Class II furcation better than class III

As the gingival recession decrease it will be better

As the width of keratinized tissue increase it will be better

Thick gingiva better

Wide interdental space better ( easy to manipulate the membrane )

As tooth mobility decrease it will be better

And good oral hygiene

- patient factors :

Systemic ; stress

Behavioral ; smoking and compliance

Local ; plaque control and residual infection after initial periodontal treatment

- predictability of the procedure depend on :

Patient factors , the objective of treatment , the defect itself and operator skill .

Good luck