

Sheet no: 7.

Refer to slide no:

Date: 30/10/2016.

Dr: Ahmad hamdan

قِيلَ لِلْإِمَامِ أَحْمَدَ :

كَمْ بَيْنَنَا وَبَيْنَ عَرْشِ الرَّحْمَنِ؟

قَالَ: دَعْوَةٌ صَادِقَةٌ مِنْ قَلْبِ صَادِقٍ.

Regenerative surgery

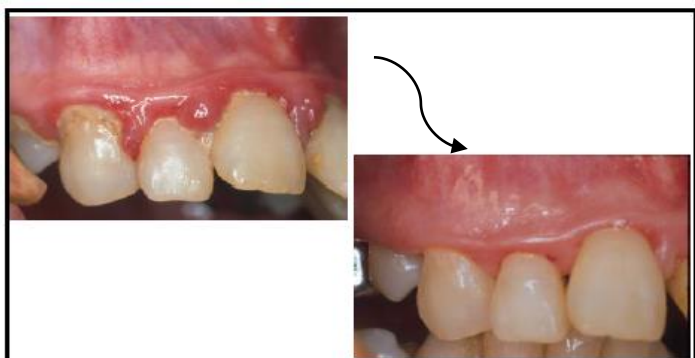
We talked in the last lectures about suturing, flaps and gingivectomy. From now, we will start talking about advance concept that depends on what discussed in last lectures. All surgery that we will learn from now depend on basic technique (gingivectomy, alveoplasty,gingivoplasty , circular incision ,,etc) . So to start today with regenerative surgery

Note: doctor did not finish this topic; I do not know if there will be another lecture about it.

Aim:

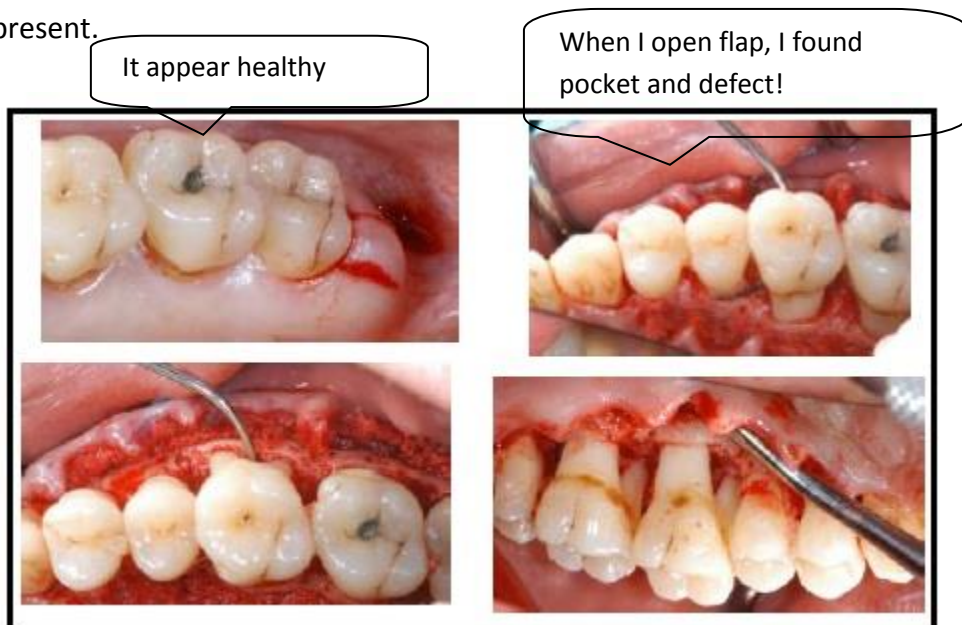
The aim of this surgery is to transfer the patient from disease state to more healthy status. Therefore, we have Control of inflammation, arresting disease process and establishing prober oral hygiene. (in periodontal disease stopping the disease process itself is not enough to maintain the success of the surgery). Therefore, you should reach with your patient to acceptable level of oral hygiene. From this point the difficulty of the regenerative surgery rises. (Such kinds of surgery need **induction of behavior change**).

So again, the aim of this surgery to transfer from status has swelling, plaque, bleeding on probing and pocket to status of health.



Using treatment modalities such as scaling and root planning, maintenance therapy, and antimicrobial therapy, this will help us to control the pathogenic microflora to prevent further periodontal destruction.

However, sometime I cannot wait; if I do all treatment modalities and I have a control of disease but there is a defect as this figure below. Despite the successful treatment (scaling and root planning was successful > no inflammation and decrease of pocket depth and there is stability in the case), but sequel of the disease is still present.



In other words, despite successful disease management, anatomic changes resulting from past disease activity often occur and must be corrected. Why? Because if they were left untreated, (even with proper oral hygiene) these defects can provide a potential harbor for the reestablishment of a pathogenic microflora **and** future risk of future disease. (These areas; such as class 3-furcation invasion, deep intrabony defect).

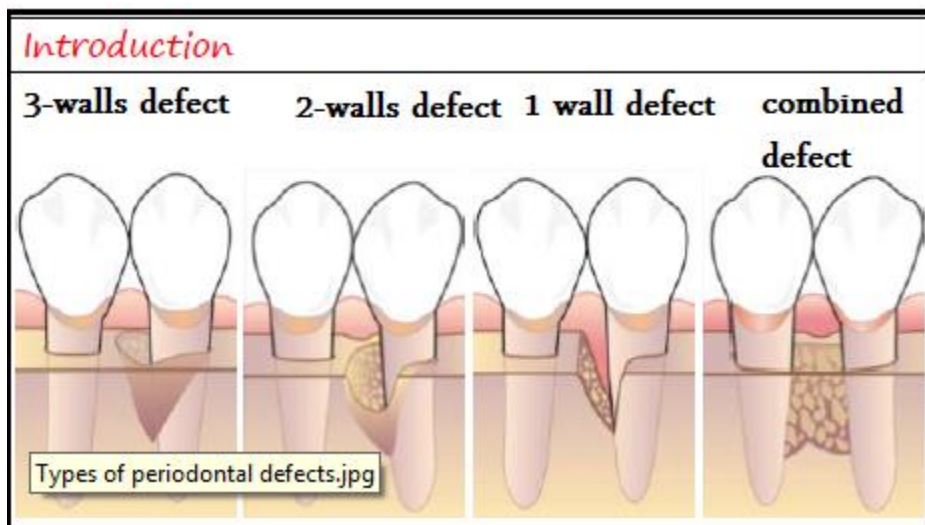
Based on that non-surgical therapy and osseous surgery can resolve some problem but not all. (e.g. defect).

- 1- Start with scaling and root planning and go to maintenance therapy; wait 8 weeks(42days) (to allow connective tissue to mature and complete the regeneration process) .
- 2- We found some pocket after treatment that did not diminish.
- 3- Management. how?

How can I manage? According to architecture and morphology of defect, I can offer my patient in more advance treatment approach which is regeneration of tissue.(remember regeneration done by many methods one of them is bone graft, you shouldn't think in bone graft as the first solution).

As a conclusion, in cases with persisting deep pockets, surgical procedures should be undertaken to clean the root surfaces. Surgical therapy:

- 1- Open flap debridement: a flap is elevated to expose root surfaces and clean them by removing all calculus and granulation tissue. (What still present here? bone defect).



- 2- Osseous resective surgery: this procedure involves osteotomy and osteoplasty to remove **shallow** vertical bone defects. This solution is not possible in cases with **deep** vertical defects because a lot of tissue loss will result from removing the deep defect.



- 3- Regeneration: this is the ideal surgical treatment modality in cases with **deep** vertical bone defects.



So either debride and leave it or osseous surgery or regeneration.

In cases with deep pockets, non-surgical therapy alone is not enough to achieve a healthy periodontium as the pockets cannot be completely eliminated. This is because deep pockets are a risk factor for further accumulation

and recolonization of bacteria and plaque and further disease progression. In some patients who are compliant, attend for a dental check up every couple of months, and have very good oral hygiene, a few pockets can be maintained without plaque accumulation if the pockets are not too deep (3-4 mm in depth) and the pockets have favorable morphology.

Principles of regenerative medicine

Medicine, in general, used to be prosthetic medicine. In other words, lost tissues are replaced by external tissues or prostheses regardless of the material of these external prosthetic tissues (whether they are made of metal, plastic, allogeneous tissues etc.).

New era of regenerative medicine has established. In which replacing metallic prosthesis to more biological approach. (Replacing missing bone by bone).

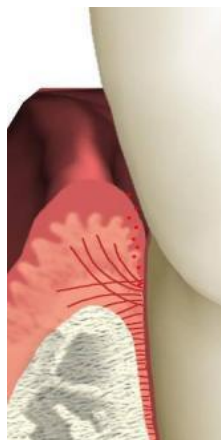
Tissue replacements come in a wide range, from prostheses replacing the head of the femur in the hip joint, to dental implants, to fixed partial dentures, and removable dentures in general. Even bone grafts are, in a certain definition, replacements. ((Even in conservative dentistry))

The aim of regenerative medicine is to get rid of all of this metallic prosthesis; because they do not provide us with the ideal treatment, which is giving function without any side effect.

Medicine is moving from being purely prosthetic towards relatively more regenerative procedures.

- **Regeneration: The reproduction or reconstruction of a lost or injured part.**
Periodontal regeneration implies the formation of new cementum with inserting collagen fibers and bone.

**** Here we should have bone, cementum and perpendicular collagen on the tooth surface.**



- **Repair: The situation in which healing does not completely restore the architecture or the function of the lost tissue or parts.**

Periodontal repair may include:

- 1- **Formation of a long junctional epithelium**
- 2- **Connective tissue attachment**
- 3- **Ankylosis.**

****based on different type of cells that will occupy the defect.**

In other words, if bone was grafted along with other growth factors but the end result was only bone formation and ankylosis without connective tissue attachments (collagen fibers), this is considered repair not regeneration.

For a process to be considered regeneration, the tissue has to go back to the way it was anatomically and physiologically before the disease (as if the disease never took place).

In normal healthy periodontal tissues, collagen fibers are inserted **perpendicularly** to the surface of the root. In repair, there will be incomplete regeneration of bone, and as a result collagen fibers will be inserted **parallel** to the root surface along with resorption of this root surface.

Periodontitis as disease happen due to loss of PDL so there will be bone resorption. Loss of PDL is the main cause and the others happen as consequence. Because if the bone loss happen without periodontal disease this will be another story!

Why is regeneration not achieved in some cases?

A space will be created in the periodontium because of the tissue loss. This space should be occupied by a tissue. In the area surrounding a tooth, four tissue types are available; cementum, gingiva (epithelium), connective tissue, and bone. Everyone has a special metabolism speed and special turnover speed; based on its function, its energy and its genetic program.

Healing happens after defect, our bodies try to heal the space (defect), but most time they fail. Why? Because of the difference between the tissue.

Epithelium has the **highest** tendency to fill the space created by tissue loss, since it has the **fastest growth rate**. If epithelial growth is restricted, connective tissue will proliferate and fill the space since it has the second fastest growth rate among these four tissue types. If connective tissue growth is restricted, bone will tend to

grow and fill the space (ankylosis). Cementum is the tissue that grows at the slowest rate among the four tissue types. If pdl is allowed to grow in natural manner then regeneration will happen. From here the complexity of this procedure rises, there is no way to allow every tissue to work within limit and in limited period!

Epithelium migration needs basement membrane, so it happens below the clot not above. And under the granulation tissue. (viva question)(plz check doctor , ana mo mt2kda 100% and write it on facebook group l2no l check **wound healing** lecture bs mo mt2kda eno hek tartebhom.

Epithelium is the fastest due to its function that is protection (physical barrier).

Embryologically, the periodontium develops in the same sequence: epithelium is formed, followed by connective tissue fibers, then bone, and cementum is the last tissue to develop as the tooth starts to erupt. Cementum is the most specialized tissue and needs a longer time to form.

Because of the presence of these four different tissues that are competing on the same space created by tissue loss, there are 4 possibilities to end up with (as mentioned above):

- 1- Formation of a long junctional epithelium
- 2- Connective tissue adhesion accompanied by some degree of root resorption and insertion of connective tissue fibers parallel to the root surface.
- 3- Root resorption and ankylosis. In this case, bone is in direct contact with the root surface.

The first three points are considered repair.

- 4- Regeneration, which involves the formation of new bone, cementum, epithelium, and connective tissues in the correct proportions. (cementum cannot regenerate itself, its regenerative cells present in pdl).

If the regenerative procedure was not successful, repair will take place with a combination of the first three processes, meaning that in some areas there will be a long junctional epithelium, with some areas containing connective tissue adhesion, and other areas will contain bone formation and ankylosis, with regeneration seen in some other areas as well.

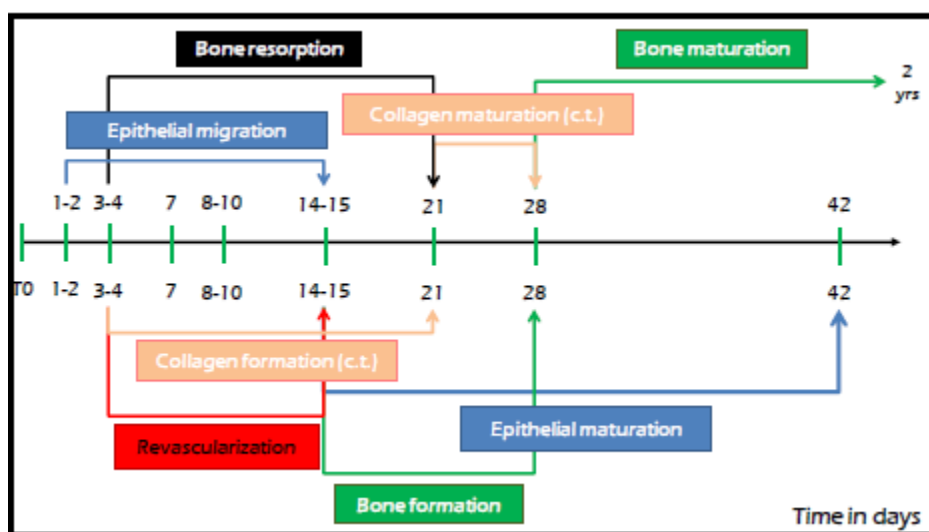
Epithelium migrates apically with the help of the connective tissues. Once it migrates apically and produces a long junctional epithelium to occupy the defect on the root surface, it will cover the root surface and **prevent the regeneration** of the proper periodontium.

Clinically it is impossible to tell the difference between regeneration and repair by probing. Repair and regeneration can only be differentiated histologically.

The process of regeneration includes: epithelial migration and maturation which takes place first as it is the fastest, followed by connective tissue formation (collagen fibers), and then revascularization takes place. Bone resorption takes place within the first 21 days, and bone formation starts during the first 2 to 4 weeks. Bone maturation needs more than 2 years to occur. Epithelium maturation happens after 42 days that is why we give 8 weeks as time of reevaluation of non-surgical therapy (after root planning).

This shows that regeneration is a dynamic process and it depends on many factors. The two most important factors are:

- 1- The chemical stimuli that are present in the area
- 2- Metabolism; bone is one of the most involved tissues in the metabolism and balance of electrolytes.



** (This is according to healing model in animal not in real human!)

Techniques used to achieve regeneration

1- Root conditioning procedures

Initially, it was thought that if the root surface was conditioned and cleaned this will enhance the cellular activity that is needed to achieve regeneration. (So if we treat the surface, the tissue will be able to function correctly).

The two agents that have been studied the most regarding root conditioning are **(a)** EDTA in low concentrations and **(b)** Tetracycline. It was thought that tetracycline adsorbs to the root surface and stimulates stem cells or regenerating cells to migrate to the defect site and bring about tissue regeneration. This scenario was proved in in-vitro models and in animal studies. However, in all the human studies **except one** case report, the results were negative. **(dr told us to read the paragraph that related to these material in the book, there will be a question about them.)**

In conclusion, this technique and these materials should not be used because they are not supported by evidence of success in human studies. They are only successful in in-vitro and animal studies which is not enough to advocate their use.

Often, studies may give positive results in-vitro and in animal models and higher primates (monkeys) but will give negative results in human studies.

2- Bone grafts and bone substitutes

This is the second technique that may achieve regeneration. Bone can be grafted using bone or bone substitutes. **Any graft material other than autogenous bone is considered a bone substitute.** This is because bone is a tissue and by definition, a tissue contains vessels, cells, growth factors, and matrix (and autogenous bone is the only graft material that contains all these components). Bone grafts from allogeneous sources do not contain vessels or cells; it only contains matrix and one growth factor.

Signals molecule and saving space.

3- Guided Tissue Regeneration

This concept involves the guiding of the regeneration of tissues according to their rate of turnover. (Interfering with the natural sequence).

4- Biologic and biomimicry mediators

This concept was developed in the late 90's. It involves the use of certain growth factors that will target such cellular activity which will help to induce a certain step of the regenerative process. The regenerative process has three main requirements that:

- (a) Regenerative space: the space created by the bone defect needs to be maintained. Otherwise, if the space is left as it is, it will be quickly occupied by epithelium within the first 14 days while bone starts formation at 14 days.
- (b) Signaling molecules: the space needs to be provided with the necessary signaling molecules. There are no less than 500 to 600 molecules that are involved directly or indirectly, in a very active manner, in the formation of bone and cementum. The same molecule may affect more than one cells type. Also, a single factor may have either a stimulating or inhibiting effect a cell depending on the stage of cell development. It is a very complex process. (Such as **TGF- β 1**, igf ,etc.)
- (c) Stem cells (progenitor cells) ((major player))

In order to obtain regeneration, all three conditions need to be met. (If anyone of the 3 factor above was missing then it will repair!)

The objective of treatment should always be regeneration. However, due to the complexity of this process, regeneration is not always possible in most of the cases.

Assessment of wound healing

Wound healing can be assessed in one of the following ways:

- Probing depth
- Clinical attachment level
- Bone fill
- Histological analysis

1- Probing depth: it depends on inflammatory state of the tissue, If it was inflamed it will lead to penetrate .5mm apical more than the connective tissue seal. (sulcus depth + .5mm). If the tissue healthy then the probe have a tendency to stop coronally 0.5mm to the connective tissue seal. ((.5mm is average, not the exact reading)).

This is **not a reliable** way of evaluating regeneration vs repair; because it is only a clinical evaluation of the presence or absence of pockets and depth of these pockets. Whether there is a long junctional epithelium, or ankylosis, or regeneration, all three scenarios will present as attachment gain clinically and cannot be differentiated by probing.

2- Clinical attachment level: this method of assessment is more reliable than the probing depth; however, it is not completely reliable. It is more reliable than probing depth assessment because probing depth relies on the level of inflammation of the gingiva at the time of probing. Clinical attachment evaluation involves the measurement of the amount of gain in attachment by evaluating the difference between the post-operative probing depth and the pre-operative probing depth (probing depth analysis only involves measuring the pocket depth post-operatively, while clinical attachment level analysis measures it both pre-operatively and post-operatively). **This method is not completely reliable because tissue regeneration and repair cannot be differentiated from one another, the type of repair cannot be assessed, and there may be some degree of gingival recession (not only attachment gain) which may give false results.**

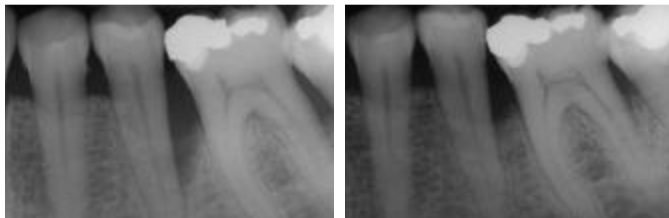
Note: A pocket depth of 5 mm will, for example, be reduced to 3 mm after non-surgical periodontal treatment. This 2 mm decrease in probing depth is a combination of both attachment gain (1.25 mm) and gingival recession (shrinkage of inflamed gingiva by 0.75 mm).

So again here we can know if there is any reduction in pocket depth, but we cannot know the type of the tissue and whether the reduction happens because of shrinkage of tissue or because of gaining tissue, and if we know that reduction happens due to real gain, I cannot know what type of gain I have.

3- Bone fill: this can be assessed by several methods;

- Surgical re-entry to the area and visually assessing bone formation
- Taking reproducible parallel technique radiographs to assess bone formation
- Anesthetizing the gingiva locally followed by bone sounding (probing the bone through the gingiva)

Bone fill does not allow the clinician to differentiate between regeneration and repair, as there is a possibility that ankylosis has occurred. Another possible scenario is the formation of a long junctional epithelium along with bone formation.



Advantage: 1- minimal invasive 2- indication (what happens) 3- quantifying (somehow) (**Subtraction technique**) (صورتين اقرب ما كونوتا لبعض وبحطهم على بعض وبشيل كل اشي والفرق بينهم بيطلع)

Disadvantage: 1- I do not know where is the attachment happens.

4- Histological analysis: This is the only method that **can reliably be used to differentiate between regeneration and repair**. It is possible to determine if the periodontal ligaments have been regenerated and if the connective tissue fibers are inserted perpendicularly to parallel to the root surface. The problem is difficulty in making .

Some studies that made on animal and human they found that no way to find one type of attachment after healing. Which means that the process is so complex. (انا ما بعرف اذا فهمت الاشياء الي كتبتهم صح مثل ما حكاها)
(الدكتور !)

Bone Grafting Materials

Bone grafting materials can be autogenous, allogeneous, xenogeneous, or alloplastic materials. These materials differ from one another in their source.

Terminology: (according to its activity)

- Osteogenic: the graft material itself produces the new bone. The graft completely contains bone-forming capacity.
- Osteoinductive: the graft material induces bone formation in an ectopic site through chemical factors. The graft contains cells for bone formation, but stimulating factors from the graft site are needed to complete the bone formation.
- Osteoconductive: the graft material acts only as a mechanical scaffold for cells to migrate and form bone. This type of bone graft only fills the space of the defect and depends on the bone forming capacity of the defect site to accomplish regeneration. Scalloped allow adhesion

Osteogenic bone grafts are the best materials for regeneration while osteoconductive bone grafts are the least useful.

Bone substitutes should lead to regeneration but in reality they lead only to repair. This is because the environment of the periodontium is very complex.

Theoretically, bone graft materials should be resorbable. The rate of resorption should coincide with the rate of natural bone formation. However, almost all bone graft materials are not completely resorbable in the human environment, ending up in areas where the graft is resorbed and areas where it isn't. The reason for this discrepancy in resorption is not related to the graft material itself; **it is related to the difference in oxygen availability between different areas of the graft.** **The stem cells that attach to the bone substitute have special properties. One of their most important properties is their ability to support hypoxia for up to 7 days.** Stem

cells are very plastic cells and can either increase or decrease their cellular activity and need for energy and oxygen depending on the amount of oxygen available in their environment. On the other hand, oxygen from the vasculature cannot penetrate deeper than 200 microns into the graft material, and this has been shown by microscopic dynamic studies. So, in superficial areas that are close to blood vessels, the bone substitute will be resorbed and replaced by natural bone. In the deeper areas, the graft material will not be resorbed as the stem cells will die due to the persistence of hypoxia for more than 7 days. Instead, the deep site will end up with fibrous tissue formation.

An ideal regenerative material should include cells, a scaffold, and signaling molecules.

- **Autogenous bone grafts** are osteogenic because they contain cells, a scaffold, and signaling molecules (3 part needed for regeneration). The scaffold in this case is important in maintaining the regenerative space that is needed for regeneration (as mentioned above). Sources for autogenous grafts can be either intraoral or extraoral.

Extraoral sources include flat bones such as the iliac crest. Extraoral sources have disadvantages because they are a secondary surgical site, they are associated with morbidity, and they are a limited source for bone grafts. If a bone graft is taken from an extraoral flat bone, another graft can only be taken from the same site for a second time because flat bones do not have a high capacity for regeneration. Long bones are weight-bearing bones and bone grafts are never taken from them.

Intraorally, bone grafts can be taken from edentulous ridges, maxillary tuberosities, mandibular ramus, tori and exostoses, and the anterior mandible. (the most from mandible, the problem is that the mandible is cortical so no presence of blood supply, so resorption is more due to less number of cells).

The disadvantage of intraoral graft materials compared to extra oral sources is that the intraoral grafts have a higher proportion of cortical bone.

Iliac bone is the best material available for bone grafts regarding physiology and biology due to its ideal structure. However, clinically it is not the best option because it is not practical to take a graft from the ilium using a secondary surgery and damaging the ilium in order to treat a vertical bone defect. Iliac bone **can achieve a bone fill of up to 4 mm**.

Iliac bone and DFDBA (discussed below) are the only graft materials that can achieve regeneration of periodontium in cases with horizontal bone loss (zero wall defects)((reported evidence)). However, this was only reported in two cases, in a small number of patients, with the work of one of the most skilled periodontal surgeons in the world.

- **Allogeneous bone grafts** contain a scaffold and signaling molecules; they lack stem cells. They are **osteoinductive** and depend on the cells that are present at the site of the bone defect for regeneration.

There are two types of allogeneous bone grafts: **DFDBA** (demineralized freeze dried bone allograft) (demineralized = signal molecule) and **FDDBA** (freeze dried bone allograft)(dried=no fluid)(freeze=to protect it).

Theoretically, the disadvantage with these allografts is the probability of disease transmission between patients. In other words, if an allograft is taken from a patient with a certain disease such as HIV or HBV, there is a possibility that this disease will be transferred to the recipient of the graft. However, this has never been reported in the literature and disease transmission has never happened in any cases clinically.

Therefore, in reality, it is a safe option. Its advantage is that its composition is hydroxyapatite, which is very close to the natural bone found in humans, and it also contains BMPs (bone morphogenic proteins) which enhance the bone formation.

DFDBA (demineralized) is a better option because it is more easily resorbed and release of bone morphogenic proteins from FDDBA is easier.

The osteoinduction of allogeneous bone grafts depend on: extent of demineralization of the graft, age of the donor, and cell proliferation and alkaline phosphatase activity of the host cells (the cells that are present in the site of the bone defect). In other words, osteoinduction and formation of new bone heavily depends on the cellular activity of the host. Studies have shown that active bone gain using allogeneous grafts can be maintained for up to 3 years. **DFDBA has been shown to regenerate bone in cases with horizontal bone loss.**

<p style="text-align: center;">شمس التبريزي</p> <p style="text-align: center;">قونية، ١٢ حزيران (يونيو) ١٢٤٥</p> <p>مؤمن مضطرب! إذا صام المرء شهر رمضان كلّه باسم الله، وقدم خروفاً أو عنزة كلّ عيد ليغفر الله له ذنوبه، وإذا جاهد المرء طوال حياته ليحجّ إلى بيت الله الحرام في مكة المكرمة، وإذا سجد خمس مرات كلّ يوم على سجادة صلاة، وليس في قلبه مكان للمحبة، فما الفائدة من كلّ هذا العناء؟ فالإيمان مجرد كلمة، إن لم تكن المحبة في جوهرها، فإنه يصبح رخواً، مترهلاً، يخلو من أي حياة، غامضاً وأجوف، ولا يمكنك أن تحس به حقاً.</p> <p>هل يعتقدون بأن الله يقيم في مكة المكرمة أو في المدينة المنورة؟ أو في أي مسجد من مساجد العالم؟ كيف يمكنهم تصوّر أن الله يمكن أن يكون محصوراً في فضاء محدود وهو الذي يقول: «ما وسعني أرضي ولا سمائي، ووسعني قلب عبدي المؤمن».</p>	<p>لا تنسى أنه في زحام الدنيا قد تحدث بعض الأخطاء وقد تتكرر حدوثها بين الحينة والآخرى، في كوننا الصغير الذي يقبع في الشرفه التحتيه للمستشفى تتكرر بعض الأخطاء فلقد بان للعموم بأن تلاشت صور التسامح بيننا فترانا حيننا نترصد أصغر الكلمات ونستقصدها سوءاً أو ترانا نتألفت أين يقبع احد الدكاترة ليساعد شخصاً فترانا يشط قلبنا غيضاً نحمل ما أوتينا من تهيؤات وخزعبلات واحاديث جانبية نلقي بها هنا وهناك، هناك من يحتكر المرضى وهناك من يفسد فرحتنا بأدواتنا، لم يعد من الجميل أو اللائق حتى ان نغدو هكذا فللكون الصغير هذا محيط توجد به شمس وسماء وارض عليها تنمو شجيرات واعشاب في كل سنة تموت ثم تحيا من جديد .</p> <p>أن من الجميل ان نتصالح مع انفسنا وان نقرر من نحن ، اذا لم نستطع ان نتخلص من أنانيتنا (حتى انانيتنا واحنا بنشكي بعض) فاننا لن نصل لمرحلة أملاكنا المحبه !</p> <p>قال رسولنا الكريم : لا يؤمن أحدكم حتى يحب لأخيه ما يحب لنفسه.</p> <p>لو وصلنا لمرحلة بنقدر نحكي لبعض المشكلة الي حاسينها تجاهم رح تفرق بكثير عن انه عم نحكيها لاي حد بالدنيا الا هم انفسهم و اخر دعواهم ان الحمد لله رب العالمين .</p>
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