Sheet no.: 24
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Corrected by: Linda Morgan  ***Why is it necessary to know about periodontal wound healing?!***

Our goal is to try to restore everything back to normal, which means that it’s important to understand the process in order to know how to do our treatment procedure.
We have to know exactly what happens so when I get to do a certain procedure it will be based on the relations that occur through the healing process, and this helps us restore tissues that would be similar to the normal tissues which used to be in the normal condition.

\*\*The doctor recommends everyone to read chapter #3 especially the people who are interested in majoring in surgery, periodontology or interested in stem cells.

Periodontal wound healing is not that much different from cutaneous wound healing. It has some special features that characterize it. First, the **environment is very complex**, Why?! Because there is contact between multiple tissues, also contact between tissues and the external environment.

There are **several factors** that differ the periodontal wound healing from cutaneous wound healing:
1. Continuous contact that couldn’t be obliterated between the tissues and the external environment.

2. Multiple tissues and origins that are available. Four different tissues participate in the formation of the tooth socket (Epithelium + Gingival connective tissue + Alveolar bone + Cementum ).

 3. Different organization between the tissues.

4. Healing of a **vascular** gingiva with the **Avascular** root surface which makes it more challenging and complex (while in cutaneous wound healing, healing occurs between two vascular parts which makes it easier).

5. The microbiological content & aggregation (bacteria , fungi ….).

6.The presence of many Junctions ( such as ; dentino-cemental junction , dentino-enamel).

\*\* I copied factors #2, #5 and #6 from last year’s sheet.

Development of periodontium is a very complicated process that makes healing even more difficult because it includes many cells and interactions. So I have to understand the process that occurs during regeneration and compare it with the developmental process so I can get the consensus points between both processes and the differences as well and then try to get over the differences.

We have certain differences between what happens during development and what happens during regeneration. However, the events are the same since the healing process from a physiological point of view is considered a formation process or reformation process.

The events are:
Migration Adhesion Proliferation production of the extra cellular matrix and in case of mineralized tissues this matrix will be mineralized.

The differences are identified at the **cellular level**. We have different cells that are involved in the formation ***(development)*** of the tooth and the periodontum which are:
1.Follicular cells
2.Odontoblasts
3. Neural cells
4.Herwig’s epithelial root sheath cells
5. Endothelial cells
6.Stem cells
7.Osteoblasts
(The Dr said:“no need to memorize the cells but it’s important to know the function of them”).

On the other hand, ***during regeneration*** we can find some of the cells mentioned above except the **neural crest cells.**

What really makes the MAIN difference between the development and regeneration process are the ***inflammatory cells.***

Inflammation is a very complicated process that is present for an essential purpose. However, this inflammatory process makes our job and the way to treat the tissues harder, and also the desired results become even more difficult to get.

***Development vs. Regeneration***

***Development****:*

What happens during development at first is the ***cellular condensation***; the cells accumulate at certain place, and ***spatial reorganization*** then occurs in the space and the target. Under the influence of certain factors we will get the ***progenitor cells.*** And under the influence of certain factors that are different from the previous ones (though they have some in common) we will get the ***differentiated cells*** and ***functional organs.***

***Regeneration****:*

First thing happens is the ***formation of blood clot*** (this part shows a big difference from the developmental process) then the blood clot has to be degraded (***degradation and remodeling***), then ***granulation tissue*** will form then we’ll get the ***progenitor cells from the stem cells*** (under the influence of certain factors; migration, adhesion, and proliferation factors).

\*\* The doctor tried to break this down by giving an example:
If you extracted a tooth, there will be a space that will be filled with blood clot, then this clot will be degraded and remodeled to form granulation tissue, then under the influence of certain factors the stem cells will be differentiated into progenitor cells in an attempt to reproduce or regenerate the lost tissues except for the dental organ.

\*\* a student asked: from where do we get the stem cells?
mainly there is in the body something called perivascular niche (niche in Latin means عش) it’s like something accumulates in certain areas. And the same way is the stem cells which accumulates around the blood vessels in certain areas in a form of niche.

After getting the granulation tissue, all the processes that come after are the same in both processes (regeneration and developmental). These are the same factors that influence the stem cells to produce progenitor cells, and we have almost the same factors that are leading to the production of tissues and replacement of lost organisms.

The difference between formation (development) and regeneration is that the blood clot doesn’t exist in the developmental process. The main cell in the blood clot is **nuetrophil** which has multiple functions.

We need to know about the junctions in the periodontum in order to understand the healing process.

***How does the dentinocemntal junction form?***
1. Disintegration of the hertwig’s epithelial root sheath
2. Precemntoblasts communicate with the nonmeneralized dentinal matrix
3. The cementoblasts will implant collagen fibers in the predentin. Then the dentinocemental junction is formed.
4. Mineralization of the dentin, then mineralization of collagen fibers that’s found in dentin.
5. Establishment of the cemental matrix.
6. Mineralization of the dentinocemental junction.

* ***Wound healing process:***
-Primary intention: wound closed by approximation of wound margins or wounds created and closed in the operating room, Best choice for clean, fresh wounds in well-vascularized areas (not with periodontum)
* -Secondary: a wound left open and allowed to close by epithelialization and contraction,  management of contaminated or infected wounds.
* -Tertiary:  wounds that are too heavily contaminated for primary closure but appear clean and well vascularized after 4-5 days of open observation. Over this time, the inflammatory process has reduced the bacterial concentration of the wound to allow safe closure.

\*\*The above 3 points were taken from last year’s sheet because there was a long discussion that was not clear enough to be written here, and the dr asked a student to check wekipedia regarding some points.

***What are the phases of wound healing?***
1.Inflammatory phase
2. Granulation tissue
3. Wound contraction and maturation of the wound.

Wound healing contains as we all know : Trauma/incision, clot formation, inflammation, granulation tissue formation, angiogenesis, epithelialization, and remodeling.

The clot formation function is to ***protect*** the tissue, and acts as a ***matrix for cell migration*** (it’s the initial and primary matrix that will allow the migration of cells). Also it’s a ***reservoir*** for cytokines and growth factors. The clot formed by the conversion of fibrinogen into fibren on the site of injury and the accumulation of platelets as well, whereas the exposure of the platelets to the environment causes the release of the alpha granules, these are necessary for the healing and recruitment of stem cells and orientation of the tissue involved in the site of trauma.

Angiogenesis is very important. We have a process called angiogenesis and another process called neovascularization, the later means that we get blood vessels from nowhere. However, angiogenesis is the protrusion and outgrowth of capillary buds and sprouts from pre-existing blood vessels.

In the process of wound healing we have two possible end results. Either we get ***regeneration*** or ***repair (like extraction socket)***. Repair healing results quality are less than the quality of tissues used to be normally at that site before trauma.

We have two crucial factors that will decide whether we will obtain **repair of regeneration**:
1***. Availability of needed cells***.
2. ***Presence or absence of cues and signals necessary for recruitment and stimulation of available cells.***Periodontal wound healing is a very difficult process since the cells are involved come from different origins (epithelial cells from ectoderm, fibroblasts, osteoblasts & cementoblasts from mesenchyme). The bones of the head and neck are different from the rest of the bones of the skeleton; the major genes that influence and control the formation of the bones in the head and neck are different from the ones that are responsible for the rest of the skeleton.
The genes that control the head and neck bones formation called **non-homeodomain genes.** And The genes that control the rest of the bones called **homeodomain genes**. Due to these differences in genetic information and genetic program we get as a result different physiology for the head and neck especially in the alveolar process since it originates from ectomesenchyme “which means that it was at first ectodermal cells in origin then they changed their mind and took a step backward to neural crest cells then to mesoderm”. So this creates the specificity that is not present in any other part of the body. (the Dr said that the information he just mentioned above in this paragraph isn’t included in his questions, he just want us to know this to make a clear picture of this concept.)

***Blood clot formation*** is the first thing happens in the periodontal wound healing, and this happens *within minutes*. Then after *one hour* ***neutrophils will infiltrate the clot***. *After 6 hours* the ***neutrophils will line the root surface***, and then they start the decontamination of this edge. *After 3 days* we are entering the ***late inflammatory phase***, and then the predominant cells like the ***macrophages*** will start the ***debridement of the wound*** and resulting in the ***release of the growth factors*** ending up with a ***granulation tissue***. *After 7 days* the granulation tissue will start to be replaced by a ***cell rich newly formed tissue***. Then we enter the ***maturation phase*** to start ***remodeling*** until later on reaching the ***functional adaptation***.
Maturation occurs in 4 different ways in the periodontum:
1. ***Collagen bundles parallel to root surface*** and it’s called collagen adhesion. (this is **repair**)
2. ***Cementoblast*** differentiation which results in regeneration because it’s perpendicular to root surface. (**regeneration**)
3. ***Resorptive activity*** (resorption of the root surface then adhesion occurs) (osteoclast & odontoclasts). (**repair**)
4. ***Ankylosis*** (**repair**)

\*\*note: the above mentioned ways can’t occur all together at the same time. So maturation happens according to one of these 4 ways.

When periodontal reattachment happens, giant cell adherence to root surface occurs as a first step which causes resorption to the root surface, Howship’s lacunae, exposure of dentinal tubules, and denudation of dentinal matrix. In the formation of the dentinocemental junction the cementoblasts inserts fibers into the non-mineralized dentin, and to mimic this situation here the giant cells will demineralize the dentin to give the cemntoblasts the opportunity to place and insert its collagen fibers into the non-mineralized dentin then after that remineralization occurs.

We have different cells which you are not required to memorize. Keratinocytes have multiple roles and the doctor only wants us to know that every cell has different roles in different stages of healing. And the same thing applies on the fibroblasts. These cells don’t share that much in common regarding their roles.

***Bone Healing***

Bone healing starts with migration, adhesion and proliferation. First thing happens is blood clotting then inflammation and after a week soft c callus forms (granulation of ECM). After 3-6 weeks the woven bone forms, and then in the 8th week remodeling starts.

What does bone remodeling mean?
It’s a dynamic process in which bone starts renewing itself with a new bone that is laminated and can withstand forces.

In the bone remodeling process the bone at first will be resting (resting phase), then enters in resorption phase due to signals came from osteocytes to osteoblasts ( when reaching such phase the young modulus of elasticity of the bone at this stage will get to a level close to fracture, so the osteocytes sends signals to renew the bone). This process happens by presenting the RANK receptor of the osteoclast to the RANKL receptor of the osteoblast based on a message came from osteocytes to the osteoblasts, so the osteoblasts are the cells which recruit the osteoclasts. 

After the resorption phase ends, the reversal phase starts, and then the formation phase comes after the reversal phase. And then the mineralization of the formed bone happens and again we go back to the resting phase.



***What are the factors that affect periodontal wound healing?***
1. Bacterial contamination
2. Innate wound healing potential (this factor isn’t the same in everyone)
3. Local site characteristic
4. Surgical procedure/ technique
5.Intial wound stability

We always have continuous bacterial contamination through the process that’s why we shouldn’t enter into any surgical phase before establishing proper oral hygiene. So if you go for a surgical procedure and there is some calculus and plaque around, you can’t guarantee the results. “If by chance in the future you see one of the modern dentists who use facebook to show his work results, look well at the picture you might find some calculus around the surgical area he has worked on, then you can tell that this person –لا يفقه من العلم شيء-“.

Mesenchymal cells are undifferentiated cells with high proliferation rate over time and can differentiate into different cell types. They have asymmetrical mitosis; means that the mother cell gives two cells, one is more differentiated and the other is identical to the mother cell. As long as it has such capacity it’s considered as stem cell (progenitor cell). So we can get out of this mesenchymal cell a muscle, bone, tendon, bone marrow or any other connective tissue.

The regeneration of a pocket like the one shown down in the picture is really difficult because we can’t control the space. So in 1984 they came up with the idea of the **membrane system**. We put such membrane to maintain the space. SO our problem here is with the space because you can’t regenerate it easily and it’s hard to be controlled, so I have to protect the space in order to get the regeneration. Since we have different tissues (epithelium, cementum, bone …) the regeneration time differs between each one of them, the epithelium is faster than bone and cemntum. So to get reformation, I have to maintain the space and protect it from being filled with epithelium until it’s time for the cementum to regenerate. (so that’s why they came up with the idea of the membrane system). Regarding initial wound stability, every single patient should go home without any bleeding (it is a different story in extraction).

***The complications of periodontal wound healing***

The same factors that render periodontal wound healing very difficult some of them lead to the complications of the periodontal wound healing. The cause of the infection is the continuous contamination. Sometimes failure happens due to multiple specialized cell types, multiple specialized junctional complexes, avascular tooth surface and stromal-cellular interactions. So we have different tissues and factors, and also many relations, so it’s difficult to control it.

***The required steps for ideal periodontal wound healing:***
1.Elimination of infected, degraded and necrotic tissues.
2. Availability of progenitor cells.
3. Proliferation and differentiation of progenitor cells.
4. Migration to healing site.
5. Establishment of a reservoir of progenitor cells in the healing site.
6. Repopulating cells should be capable of synthesizing appropriate growth and signaling factors to restore dynamic tissue homeostasis.

In order to obtain regeneration, I have to get ***three factors***:
1. *Maintain space*.
2. Repopulate with the correct population (*Stem cells*).
3. Get the correct signals (*signaling molecules*).

\*\*If any of the above three steps is missed, then we will get **REPAIR**. If all of them are available then we get **REGENERATION**.

Good Luck ☺