The etiology of periodontal disease

Periodontal disease (whether it is gingivitis, aggressive periodontitis, chronic periodontitis) is a multi-factorial disease, in the last lecture we talked about one etiology which is PLAQUE, plaque is the main cause, today we will talk about other factors which might be implicated in the process of the pathogenesis and initiation as well as the progression of the disease specially when we are talking about chronic or aggressive periodontitis.

We might have two pts, presenting with the same related etiological factors. However, one of them have chronic periodontitis (advanced lesion ie: pocket formation), and the other one could be still in the gingivitis stage (no pocketing),this difference has many factors which could be: (1) local, (2) iatrogenic, (3) systemic, (4) genetically inherited or (5) acquired (the majority).

When we are talking about inherited periodontitis, we are not talking about classic inherited disease like down syndrome for example. Here we are talking about predisposition of the disease, this mean there will be increase in the risk to have the disease for that pt.

Microbial challenge

Host + immune- inflammatory response

Clinical sign of disease, initiation and progression

Clinical sign of disease, initiation and progression

Microbial challenge

**A B**

Environmental and acquired risk factor

**C**

Cytokines & Prostanoids

Clinical sign of disease, initiation and progression

Connective tissue and bone metabolism

Host + immune- inflammatory response

Microbial challenge

PMNs

Abs

Antigen

**Matrix- metallo-proteases**

Lipopolysaccharide

Other virulence factor

Genetic risk factors

In the past (A) ,they thought that the effect of microbial challenge on the tissues will cause the clinical signs and symptoms of the disease (initiation and progression) , then (B) they understood that there’s a mutual interaction between host-response ( immune response) and bacterial plaque, and the net result of this interaction will give us the clinical signs and symptoms of the disease (the signs are mainly related to the host).

Nowadays (C), we know that microbial-challenge will affect the immune inflammatory response, and the host immune inflammatory response will affect the metabolism of the connective tissue and the bone, but that’s not the only cause of clinical signs of the disease we have many other factors that are implicated in the process, some of them are environmental and acquired and some of them are genetic.

Like any other multi-factorial disease, this disease is related to our life style (civilization that we live), we have a number of environmental, physical and psychological factors that might alter the immune response and result in more sever periodontal disease expression, but NEVER in the initiating of the disease, for example diabetes can’t cause periodontitis, it a risk factor for the initiation of the disease ( but not necessarily that every diabetic pt will have periodontitis).

\*again 🡪 the only initiating factor for plaque induced gingivitis, chronic + aggressive periodontitis is plaque, but you can add depending on your pt diabetes and smoking.

Stress has recently implicated in the progression of periodontal disease.

Systemic factors can be categorized into modifiable and non-modifiable.

1-Modifiable:

A-diabetes

B-smoking

C-stress/psychological factors

2-Non-modifiable:

A-genetic factor (genetic predisposition: mean increase the susceptibility)

B-puberty, pregnancy & the menopause

C-Gender

D-Age

They will affect:

1-physiological response

2-vascular system

3-inflammatory response

4-immune response

5-tissue repair

They also have the potential to **modify:**

1-susceptibility to disease

2-clinical presentation of the disease

3-plaque microbiota (plaque deposition)

4-disease progression (tissue loss and destruction will be faster in heavy smokers and diabetic pts)

5-response to treatment (worse)

**Diabetes Mellitus:**

Type 1:

-destruction of insulin beta cells

-10-20% of patients with DM

Type 2: which is our concern because type 1 is mostly genetic and the pt take insulin since childhood, most of these cases we deal with them as if the pt has nothing.

Type 2 is mostly acquired (has also genetic predisposition), and many of it’s risk factors are the same risk factors for periodontal disease (this include smoking, obesity, worse life style).

**Clinical symptoms of type 2 are:**

1-Hyperglycemia

2-Polyurea / polydypsea/ polyphagia

3-Pruritis (urge to itch)

4-Weakness and fatigue

**Complications of uncontrolled diabetes:**

All of them are related to microvascular and peripheral neurons

1-retinopathy 🡪microvascular and peripheral neurons

2-nephropathy 🡪more to the microvascular

3-neuropathy (not central neuropathy, but the loss of sensation on extremities)

4-macrovascular disease 🡪this leads to CVDs , atherosclerosis and stroke.

5-genaralized impaired wound healing ~(specially fractures and cut wounds and ulcers )

6-periodontal disease (included since 2004)

**Oral and periodontal effects:**

1-Diminshed salivary flow

2-Increased burning mouth or tongue

3-Xerostomia (more related to oral hypoglycemic drugs for long time rather than diabetes itself)

4-Candidiasis

5-Clinical attachment loss

\*The effect of diabetes on periodontal tissue starts with the insulin resistance.

Insulin resistance is due to obesity (they have inherent resistance to insulin ).

Resistance leads to Hyperinsulinemia and Hyperglycemia resulting in diabetes type 2. Since obesity leads to accumulation of glucose in high amounts over long periods of time so no more enough space for glucose so the body eventually converts glucose to triglyceride (fat) causing Hyperlipedemia and LDL, leading to heart diseases.

Hyperlipedemia >> increase CRP (C - reactive protein: one of the acute phase response protein)>> works on the liver >> causing increase in the production of inflammatory cytokines >> increase TNF-alpha and TNF-alpha itself affects many systems>>decrease anti-inflammatory factors which are PDGF (platelet derived growth factors), TGF-B1, BFGF (basal fibroblast growth factor), and this will help in the initiation and progression of periodontitis.

Obesity

TNF-alpha

Liver

Insulin resistance

High CRP

Hyperinsulinemia

Hyperglycemia

Hyperlipedemia

High CH , high TG

Type 2 DM

Heart diseases

Periodontal diseases

\*Hyperinsulinemia and hyperglycemia 🡪 type II diabetes.

\*Hyperlipedemia🡪 affecting CR-P and TNF- alpha 🡪leads to heart disease.

\*Both Hyperinsulinemia/ hyperglycemia and Hyperlipedemia have an INDIRECT effect on periodontal disease.

So in diabetes the LDL and TG will be increased and that will cause impairment to tissue response through the alteration of the immune response:

* increase IL-1B, TNF-A by monocytes, and this by it self will help in the increase of plasmatic level of TG and LDL.
* Increase IL-1B, TNF-A by PMNs
* Decrease PDGF, TGF-B1, BFGF by macrophages (anti-inflammatory/repair tissue decrease) 🡪 increase the periodontal disease

Periodontistis by itself also leads to increase in IL-1B, TNF-A

Plaque will increase the inflammation, and the diabetes(which called inflammatory disease) also will increase it >> which leads to exacerbations of periodontitis >> that leads to systemic disease/ metabolic disturbance >> Diabetes is affected through genetics/ high fat diet >> that again causes an increase in LDL/TRG if not controlled >> and the cycle repeats

High LDL/TRG

Impaired tissue via immune cell alterations:

High IL-1B, TNF-alpha by macrophages

High IL-1B, TNF-alpha by PMNs

Low PDGF, TGF-B1, BFGF by macrophages

High LDL/TRG

Periodontitis

High IL-1B, TNF-alpha

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Diabetes

Genetics/high fat diet

Augmentation of serum lipids

Impairment of tissue response

Systemic diseases

Metabolic disturbances

Exacerbated periodontitis

High IL-1B, TNF-alpha

Pathogenic bacteria >> cause periodontal disease & poor metabolic control >> affect on the periodontal disease( have minor effect on the control of diabetes because it will increase the lipids) at the same time diabetic complication increase the pathogenic microbes

**Modifications of Host- Bacteria relationship in diabetes:**

* Effects on microbiota: anaerobic bacteria will benefit from the environment in the cerium of pts who have uncontrolled diabetes, increase of the proportions of pathologic species.
* Effects on host response: affects the functions of PMNs (polymorph nucleic cells) , cytokines from macrophages and monocytes and connective tissue.

Effects on PMNs:

Reduced function

Defective chemotaxis

Increased collagenase activity in crevicular fluid

Increased levels of β–glucoronidase & elastase (which are enzymes implicated in the destruction of extra-cellular matrix metalloprotiases).

Effect on Cytokines (monocytes and macrophages):

1-Increased level of IL-1B, PGE2 -prostaglandin- in crevicular fluid

2-Increased release of IL-1B, PGE, TNF-A by monocytes

3-Occur binding of AGEs (Advanced Glycation endproduct) to macrophages and monocytes (in diabetes complicated there’s no more enough space so start binding with macrophages) >> leads to destructive Cell Phenotype:

A-Increased sensitivity/response to stimulus

B-Excessive release of cytokines rather than the stem cells needed for repair.

Effect on Connective Tissue:

1-Reduction the growth, proliferation and differentiation of fibroblasts and osteoblasts (FB/OB)

2-Decreased matrix synthesis by fibroblasts and osteoblasts

3-Formation of reactive oxygen species damaging cellular function

4-Altered collagen metabolism due to accumulation of AGE (more degradation, low formation)

\*\*AGE leads to vascular changes leading to thickening of capillary basement membrane thus relation of diabetes to atherosclerosis

Effect on Healing and treatment response**:**

1-Decreased synthesis of collagen by fibroblasts (less attatchment)

2-Increased degradation of the collagen in the extracellular matrix by collagenase

3-Glycosylation of existing collagen at wound margin (glycosylated collagen not as strong as normal collagen & it’s a sign of the aging of the fiber)

4-Defective remodeling and rapid degradation of newly formed collagen fiber

Modifications of the host bacteria relationship in Diabetes

Tissue destruction

Enzymes

(Elastases, collagenase)

Cytokines

Chronic hyperglycemia

PMNs

Monocytes/macrophage stimulation

Age

Impaired chemotaxis

Capillary thickening

Altered connective tissue

(FB/OB)

Reduced migration

Impaired host defenses

Poorer healing

\*puberty, pregnancy and menopause :

We will talk about how the can produce periodontal disease specifically “gingivitis”.

Mainly the most common cause in these situations is the changes in hormones “ estrogen and progesterone”, these two hormone have effect on periodontium because they are implicated in the inflammatory process , estogen is a protective hormone against inflammation but progesterone increase the tendency to have inflammation, that’s why pregnant ladies can acquire inflammations easily.

Estrogen will: (1) increase salivary peroxidases ,(2) it will stimulate collagen metabolism and angiogenesis (3) trigger autocrine or poaracrine growth factor signal pathways

Both of the hormones will : (1) coordinate vascular responses and connective tissue turn over in the periodontium (2)have certain interaction with the inflammatory mediate.

Puberty and menstruation**:**

1-Increase in gingival inflammation regardless of plaque levels (why?) because of the presence of progesterone >> lead to increased the inflammation.

(Master hormone in pregnancy: progesterone)

2-Differences between studies (related to study designs)

prevotella intermedia; one of the periodontal pathogens that its present increases during menstruation and during pregnancy

*\*\*Prevotella intermedia use progesterone as a nutrient that’s why the inflammation increases during menstruation and pregnancey.*

Pregnancy Gingivitis***:***

Same as gingivitis but exacerbated more during pregnancy

* Increased BoP, pocket depth (PD), crevicular fluid flow
* More significant during the 2nd and 3rd trimesters
* Effect on microbiota by the increase in the growth of periodontal pathogens (P.intermedia proportions will increase the plaque of pregnant lady compared to a non-pregnant lady )

All above can be minimized by good OH

**Pregnancy:**

Effects on tissue and host response:

1-Increased capillary permeability and dilatation

2-Increased gingival exudate

3-Stimulation of PG (prostaglandin) synthesis because it induce the delivery.

4-Decreased keratinization of the gingival

5-Increased epithelial glycogen

6-Suppression of immune response to plaque:

1. Suppression of PMN chemotaxis and phagocytosis
2. Suppression of antibody & T-cell response

\*All of these changes happens in general in a pregnant lady to protect the fetus.

\*Many studies show that patients who have periodontal disease, they might be more susceptible to have premature delivery and low-weight birth babies.

Pregnancy epulis:

1-Also known as pregnancy tumor/ pregnancy granuloma

2-Pedunculated fibro-granulomatous lesion

3-Bright red, hyperemic and edematous

4-usually in the interdental papillae (mainly in max. ant. teeth) because it’s the most difficult area to clean.

5-Regression after parturition

6-Recurrence after surgical removal during pregnancy (usually in 3nd trimester).

7-Good oral hygiene and debridement (during pregnancy) is the treatment choice helps keep it in a small volume.

Menopause and osteoporosis:

1-Reduction of hormonal levels 🡪 specially estrogen.

2-Desquamation of gingival epithelium

3-Osteoporosis🡪 reduced bone density.

4-Can be prevented by hormone (estrogen) replacement therapy 🡪 there is a reduced risk of tooth loss with replacement therapy.

5-Also estrogen is an anti-inflammatory hormone

6-Effect of smoking on osteoporosis 🡪 increases the level of FSH and LH (increased the progesterone, further reduction in estrogen so reduction in bone density) even in menopause

Similar to pregnancy but less dramatic Increased gingival inflammation Increased gingival exudate Increase in tissue breakdown with long-term use.

**Tobacco Smoking**:

Effect of Nicotine:

1-Increase blood pressure

2-Increases heart disease

3-Increases Respiratory rate

4-Decrease in skin temperature

Periodontal diseases in smokers:

* Necrotizing periodontal diseases (NUG and NUP)
* Poorer oral hygiene because smokers tend to have less tendency to care about themselves (healthily).
* Higher level of periodontal destruction
* Deeper PD and large no of deep pocketing
* More attachment loss with more recession
* More alveolar bone loss
* More tooth loss
* More furcation involvement
* Less gingivitis and less BOP >>smoking at the beginning leads to vasoconstriction but chronic smokers the number of blood vessels -capillaries- (vasoconstriction is transient effect and after a long period of smoking the tissue will adapt >> so the vasoconstriction won’t be present any more however there will be reduction in the blood vessels & thickening in the vessels.

Smoking effect on plaque bacteria**:**

1-higher levels of plaque

2-higher counts of periodontal pathogens

3-higher proportions of sites harbouring periodontal pathogens

Effect on host response:

1-reduced inflammation

2-decrease in amount of crevicular fluids

3-fewer blood vessels in long term, but the immediate direct effect of smoking is vasodilation.

4-increase in the number of leukocytes in the circulation (though fewer in gingival because the blood vessels decrease so chemotaxis decrease)

5-inhibition of neutrophils, PMNs, monocytes, and macrophage function

6-generation of oxidative stress

7-alteration in migration of leukocytes

8-alteration in the level of enzymes produced by PMNs

9-alteration of function of T- and B- cells (lymphocyte)

Effects on healing and treatment response:

1-poorer reduction in PD and gain in clinical attachment loss (CAL)

2-impairment and retardation of tissue healing

That’s why we ask the pt not to smoke at least 3 to 4 days before and after the procedure so we will have better wound healing.

Best wishies…