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A lifetime of normal hormonal events and their impact on periodontal Health

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ABSTRACT

Current research has demonstrated a link between periodontal diseases and systemic conditions. Among these links, there are normal hormonal fluctuations during puberty, menstruation, pregnancy and menopause that present a biologic impact on the periodontal microbiology, the gingival cell function and vasculature, the local immune system and the process of inflammation. Usually, periodontal disorders affected by female sex hormones are of no significant permanent concern, since their occurrence is usually transient, episodic and self-limiting. Affected women will rarely lose periodontal attachment or teeth during these episodes. These disorders may, however, be annoying, worrisome, and of enough concern that patients will seek the counsel of health care providers for evaluation and treatment. These disorders were clinically defined during the International Workshop for the Classification of Periodontal Diseases and Conditions of the American Academy of Periodontology, in 1999; therefore the following diseases: puberty-associated gingivitis, menstrual cycle-associated gingivitis, pregnancy-associated gingivitis and pregnancy-associated pyogenic granuloma, were clearly described. The impact on the periodontium, from the female sex hormone production, as well as the different periodontal diseases and conditions throughout the woman's life, will be described in order to help the health care team guide their female patients to receive the proper treatment on time.

Key words: Oral health, gingivitis, periodontitis, puberty, menstruation, pregnancy, oral contraceptives, pyogenic granuloma, menopause.

RESUMEN

Recientes investigaciones han demostrado la interacción entre las enfermedades periodontales y diferentes condiciones sistémicas. Dentro de estas relaciones se encuentran las fluctuaciones hormonales durante la pubertad, menstruación, embarazo y menopausia que tienen un impacto biológico en la microbiología periodontal, la función celular y la vasculatura gingival, además del sistema inmunológico local y el proceso inflamatorio. Normalmente, las alteraciones periodontales afectadas por hormonas sexuales femeninas no suelen ser de gran preocupación ya que generalmente su ocurrencia es transitoria, episódica y autolimitante, y las mujeres afectadas en raras ocasiones presentarán pérdida de inserción periodontal o pérdida dental durante esos episodios. Estas alteraciones pueden ser también molestas y/o incómodas y de gran inquietud, de manera que las pacientes afectadas consultarán a los especialistas de la salud para ser evaluadas y atendidas.

Estas alteraciones han sido claramente definidas clínicamente, de tal manera que en 1999, durante el Congreso Internacional para la Clasificación de Enfermedades y Condiciones Periodontales de la Academia Americana de Periodoncia, las enfermedades: Gingivitis asociada a la pubertad, gingivitis asociada al ciclo menstrual, gingivitis asociada al embarazo y granuloma piogénico asociado al embarazo fueron ampliamente descritas.

El impacto en el periodonto, por la producción de hormonas sexuales, así como las diferentes enfermedades y condiciones periodontales, durante la vida de la mujer, serán descritas para así poder ayudar al equipo médico y de la salud, a guiar a sus pacientes y recibir el tratamiento adecuado en el momento adecuado.

Palabras clave: Salud oral, gingivitis, periodontitis, pubertad, menstruación, embarazo, anticonceptivos orales, granuloma piógeno, menopausia.

Introduction

Modern medicine is based in an interdisciplinary setting where health care providers know their area of expertise in depth, but, at the same time, know also that it is important to be able to understand and identify related pathologies and disorders. In so doing, patients are assured of receiving timely, adequate, and comprehensive care for their overall health. Nowhere in medicine is the interplay between medical disciplines more true than that which exists between oral, periodontal, and overall systemic health.

Indeed, emerging biologic and clinical evidence points to a close association of gingival and periodontal diseases with chronic systemic diseases such as diabetes mellitus (DM), atherosclerotic heart disease (AHD), and chronic obstructive pulmonary disease (COPD). The link between DM, AHD, and COPD, appears to be related to common inflammatory mediators produced in periodontitis.[1-4]

Inflammatory mediators are also believed to be partially responsible for the abnormal incidence of pre-term and low birth weight newborns in women with periodontitis. Indeed, maternal infections, ascending vaginal or systemic, are believed to commonly precipitate or serve as significant risk factors for pre-term births or spontaneous abortion. The risk increases in women who may be socio-economically compromised. Bacteria, particularly those in surface adherent biofilms, stimulate the production of host immunologic recognition and effector cytokines such as (IL-1b, Il-1a, and IL-6) interleukins, alpha factor (TNF-a) tumor necrosis, and prostaglandins. Further evidence of the link between infections and preterm births is the finding of endotoxins derived from the lipopolysaccharide component of the Gram-negative cell wall in serum and other body fluids of preterm birth women.[5,6]

It is then not surprising that oral infections and poor maternal periodontal health may be linked to pre-term low birth weight (PTLBW). It was reported over 12 years ago that women with poor periodontal health are several times more likely to have PTLBW babies than women who are periodontally healthy.[7] This link has been investigated widely but resolution of the issue will be difficult because of the other confounding factors of PTLBW: psycho-social, socio-economic, uterine pathology, fetal pathology, multiple pregnancies, co-existing systemic infections, and disorganization of the placenta. Even so, the association of periodontitis with PTLBW is clear and periodontitis may well prove itself to be a modifier and a risk factor for adverse events during pregnancy. Conventional periodontal therapy may reduce those risks.[8] Until more conclusive interventional studies provide information to the contrary, there is little clinical evidence to date to show that periodontal therapy will improve pregnancy outcomes.[9] The 6th European Workshop in Periodontology examined this issue exhaustively and presented a review of current findings in the Journal of Clinical Periodontology.[10]

The normal periodontium

The periodontium is composed of a group of tissues that support and protect the teeth: gingiva (epithelium and connective tissue), cementum, periodontal ligament, and alveolar bone.

From the oral surface point of view, the anatomical land marks of the periodontium are a band of keratinized mucosa (attached and marginal gingiva), a free gingival groove that separates the attached gingiva from the marginal gingiva, lining (alveolar) mucosa and a mucogingival junction that separates the attached gingiva from the alveolar mucosa.

Clinical healthy periodontal tissues consist of a uniformly pale pink gingival tissue that can vary depending on the vascularity, epithelial keratinization and pigmentation, with knife edge papillae, scalloped gingival margins, firm and resilient soft tissue consistency, and stippled (orange peel) texture; this tissue complex does not bleed upon gentle stimulation and/or manipulation *(Figure 1)*.

The alveolar bone proper, the cementum, and the periodontal ligament form the attachment apparatus of the tooth. The dentogingival junction formed by the connective tissue of the gingival lamina propria and the junctional epithelium function as a soft tissue "protective" barrier between the attachment apparatus and the potentially hostile environment of the oral cavity *(Figure 2a and 2b)*.

Classification of periodontal diseases and conditions

The American Academy of Periodontology has adopted a diagnosis and classification system developed during the 1999 International Workshop of Periodontology. In it, all gingival and periodontal disorders or conditions are categorized into eight sections.[9]

The first section describes Gingival Diseases. The most common of gingival diseases are bacterial biofilm or plaque-induced and inflammatory in nature. The clinical features of plaque-induced gingival diseases are traditionally degrees of marginal erythema (red and/or bluish-red), enlarged gingival contours due to edema and/or fibrosis, *(Figure 2a and 2b)*, elevated sulcular temperature, increased gingival exudate, and bleeding upon gentle stimulation (eating, brushing, flossing, probing).[9] These disorders may occur along with calculus deposits and halitosis.

Histologically, the gingivitis lesion is characterized as an inflammatory cell infiltrate of neutrophils, lymphocytes, monocytes; sulcular epithelial proliferation; and destruction of gingival lamina propria. In gingivitis, there is no destruction of the epithelial or connective tissue attachment, and the inflammation is only confined to the gingival tissues *(Figure 2c)*.

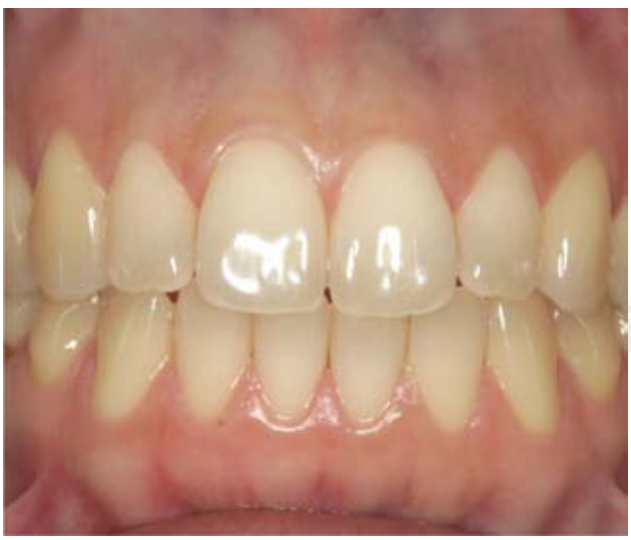

Figure 1. Clinically healthy marginal periodontium with parabolic curvature of the gingival margin.

By definition, when treated appropriately with instruction in methods of oral hygiene, scaling and tooth debridement, the signs and symptoms of most gingival diseases are reversible with no loss of periodontal attachment *(Figure 2d and 2e)*.

Characteristics of plaque-induced gingivitis[9]

1. Plaque present at gingival margin
2. Disease begins at the gingival margin
3. Change in gingival color
4. Change in gingival contour
5. Sulcular temperature change
6. Increased gingival exudate
7. Bleeding upon provocation
8. Absence of attachment loss
9. Absence of bone loss

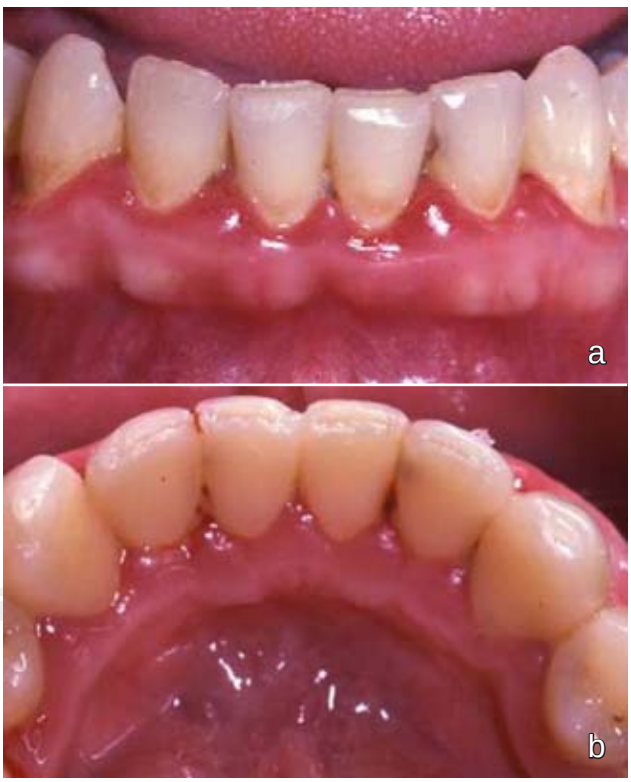

Figure 2a and 2b. Buccal and lingual clinical appearance of gingivitis with marginal and papillary erythema and edema. There is abundant plaque and calculus around the marginal tissues.

10. Histological changes
11. Reversible with plaque removal

Plaque induced gingival conditions, of which there are four, may also become modified by systemic factors. Some of the most common and most important of these are the gingival disorders associated with normal endocrine function, modified by medications, or diet and nutrition.

The classification system of gingival diseases also includes eight less common disorders that are unrelated to the accumulation of plaque biofilm. A summary of all gingival diseases appears in *table I*.

The next three sections of the 1999 classification system describe the various presentations of periodontitis. Periodontitis is the progressive loss of periodontal attachment that appears to be episodic in nature.[12] The outcomes of untreated periodontitis are compromised masticatory function, deteriorating esthetics, and ultimately the loss of teeth *(Table II)*.

The most common of these is chronic periodontitis. It occurs primarily in adults and features isolated episodic activity and slow progress. Chronic periodontitis is a bacterial infection and typically displays marginal inflammation with clinical evidence of destruction of periodontal attachment and exposed root surfaces as shown in *figure 3a and 3b*. The microbial features are complex and include the absolute requirement for specific periodontal pathogens, a conducive environment for their growth, virulence factors that allow them to evade host defense mechanisms and destroy tissue, and a susceptible host.

Aggressive periodontitis is more highly destructive of periodontal attachment and alveolar bone and usually occurs over a relatively short period of time, with what appears to be a minimal accumulation of local factors (bacterial plaque and calculus). Patients with aggressive periodontitis often display an inadequate immunologic response to pathogenic organisms.

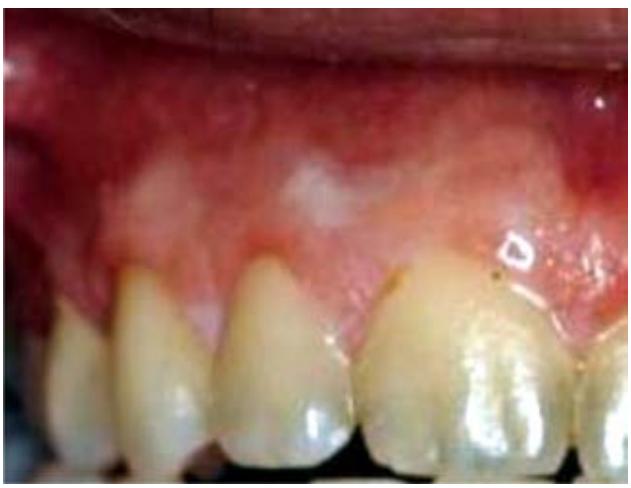

Figure 2d. Gingivitis with erythema, edema, plaque biofilm is present on tooth and mucosal surfaces.

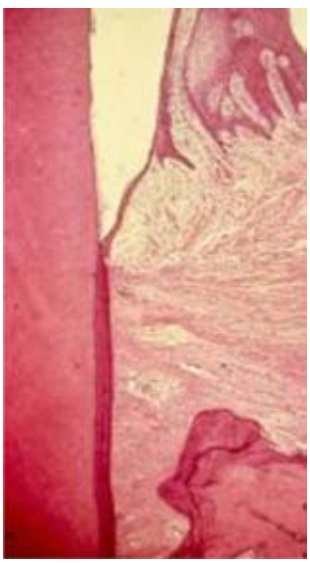

Figure 2c. Gingivitis with proliferating pocket epithelium, and inflammatory cell infiltrate.

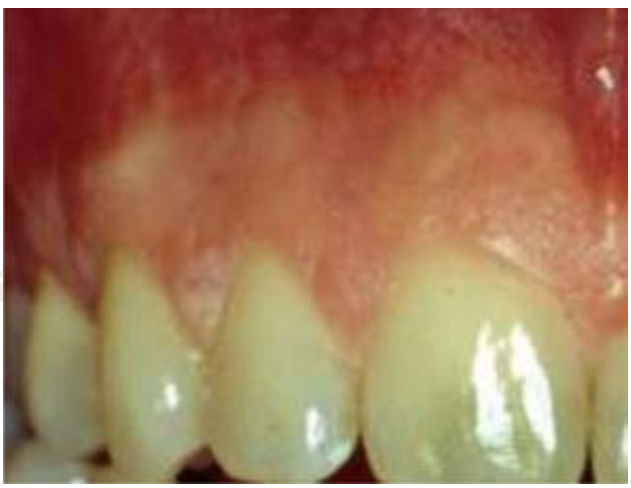

Figure 2e. Healthy gingival tissues after one week of improved oral hygiene. Etiologic role of plaque biofilm is supported.

Aggressive periodontitis has also displayed familial patterns of incidence.

Histopathologically, periodontitis portrays severe marginal infiltration of neutrophils, lymphocytes, monocytes, and plasma cells. The pocket epithelium is both ulcerated and proliferative. There is destruction of periodontal attachment with alveolar bone resorption commonly with deposits of calculus, calcified plaque biofilm, on the root surfaces. All teeth and/or teeth surfaces are not uniformly affected *(Figure 3c)*.

Necrotizing periodontal diseases (those that feature painful infection by oral spirochetes and necrosis), abscesses of the periodontium, periodontitis associated with endodontic lesions, and developmental or acquired deformities and conditions complete the classification scheme of periodontal diseases *(Table III)*.

Of the eight categories of periodontal diseases, only the gingival diseases seem most associated with endocrine functions and related medications. This does not say that the other categories of periodontal disease will not manifest endocrine influenced alterations.

Female sex hormones production

A balance of chemical mediators maintains physiologic homeostasis where variations in plasma levels impact on the patient's overall health. Among these are the female sex hormones estrogens and progestins. Accordingly, the physiology of host tissues, including those of the periodontium, is often influenced by normal hormonal fluctuations that occur during puberty, menstruation, pregnancy, and menopause.

Estrogen and progesterone receptors present in the human gingiva are believed to be responsible for the increased accumulation of these hormones in gingival tissues.[13] Cyclic increases in the production

Table I. Classification of gingival diseases.[11]

Dental plaque induced diseases[4]
Gingivitis associated with dental plaque only
Gingival diseases modified by systemic factors
Gingival diseases modified by medications
Gingival diseases modified by nutrition.
Non-plaque induced gingival diseases[8]
Gingival diseases of specific bacteria origin
Gingival diseases of viral origin
Gingival diseases of fungal origin
Gingival diseases of genetic origin
Gingival manifestations of systemic conditions
Traumatic (factitious, iatrogenic) lesions
Foreign body reactions
NOS (Not otherwise specified)

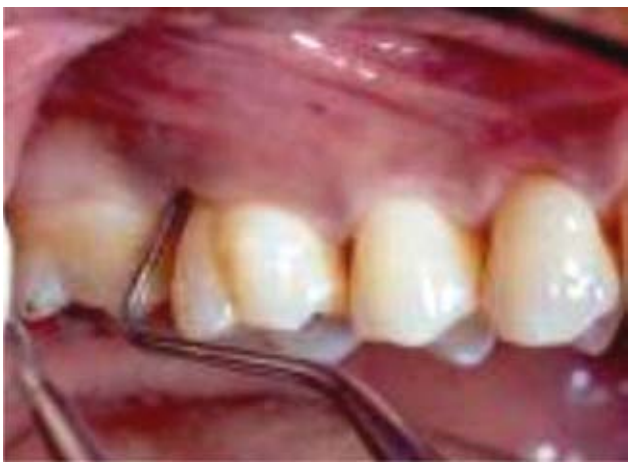

Figure 3a. Localized periodontitis showing deep probing depth tooth extrusion, and gingival inflammation.

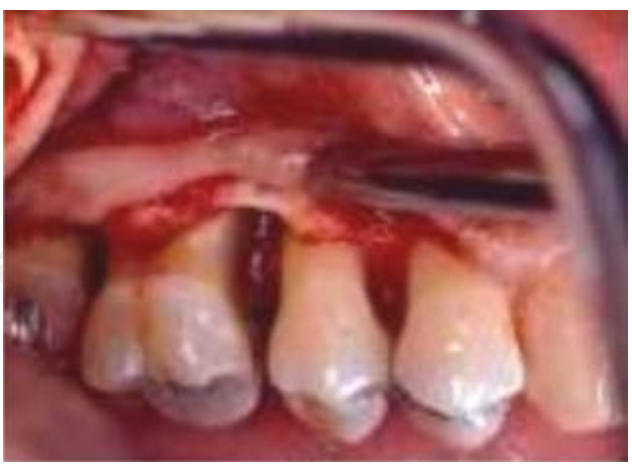

Figure 3b. Surgical exposure of periodontal defect mesial and distal to a maxillary first molar.

Table II. Classification of periodontitis.[9]
Chronic periodontitis
Generalized or localized
Slight, moderate, or severe
Aggressive periodontitis
Generalized or localized
Slight, moderate, or severe
Periodontitis as a manifestation of systemic diseases
Associated with hematologic disorders
Associated with genetic disorders
Not otherwise specified (NOS)

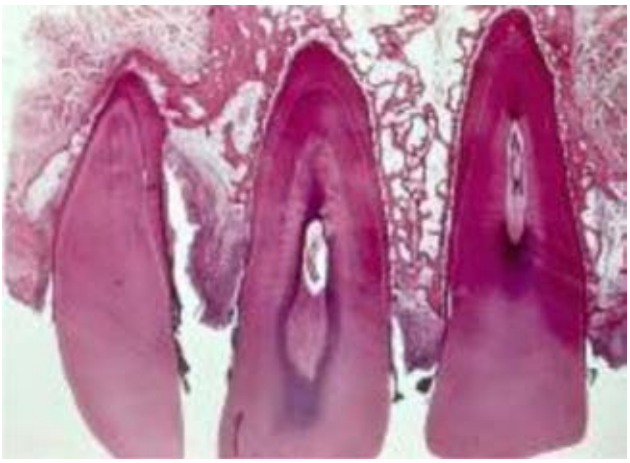

Figure 3c. Histopathology of periodontitis showing varying degrees of periodontal destruction.

Table III. Classification of periodontal diseases.[9]
Necrotizing periodontal diseases.
Abscesses of the periodontium
Developmental or acquired deformities and conditions
Mucogingival defects
Occlusal trauma

of female sex steroid hormones often alter the composition of biofilm microbiota, the biology of gingival tissue and vasculature, and recognition by effector cells of the local immune system. Commonly, the outcome is an exaggerated inflammatory response with corresponding clinical signs and symptoms in the gingiva. In addition, the changes appear to be excessive and not ordinarily explained by the amount of plaque biofilm alone.

The effect of female sex hormones on the periodontal microbiology

In the oral cavity, we can find more than 700 different bacterial species, out of which some of them have been identified to affect directly on the gingival and periodontal tissues. They will coaggregate and organize in to complex biofilms, forming organized communities. Some of them are constantly found together as clusters of pathogenic and non-pathogenic or even beneficial bacteria in plaque samples taken from patients with gingival and periodontal diseases. Typically, non-pathogenic species cluster as gram-positive, facultative anaerobic filaments and cocci (*Actinomyces* and *Streptococcus* species). Pathogenic species are seen to cluster as Gram-negative, anaerobic rods (*Porphyromonas gingivalis* and *Tannerella forsythia*) and spirochetes (*Treponella denticola*).[14,15]

At puberty, increases in the production of estrogen and progesterone occur which remain at high levels throughout the period of reproductivity. Typically, the numbers of P. *intermedia*/*nigrescens* and *Capnocytophaga* species increase in gingival tissue when estradiol and progesterone are elevated during puberty.[16-18] It has been postulated that estrogen and progesterone act as substitute vitamin K growth factors for these and other black pigmented *Bacteroides* species in plaque biofilms.

High levels of *P. intermedia*/*nigrescens* and *P. gingivalis* also occur during pregnancy corresponding to a tendency for pregnant women to display increased signs of gingival inflammation. During postpartum, lower numbers of *P. intermedia*/*nigrescens* will be recovered in gingival samples along with an observed decrease in gingival inflammation. During pregnancy the increased severity of gingivitis and gingival bleeding may occur without any corresponding increase in plaque biofilm. This is particularly

true during the second trimester. Microbial analysis of plaque biofilm in pregnant women shows an increase in the proportions of *P. gingivalis* and *P. intermedia/nigrescens* in conjunction with the increased levels of estradiol and progesterone, when compared with the first and third trimester.[19]

The effect of female sex hormones on the gingival cell function and vasculature

During pregnancy, female sex hormones may reach tissue concentrations 10-30 times that of normal. Estrogen may be responsible for alterations of homeostasis of epithelium, connective tissue, vascularity, and production of keratin and collagen. Indeed, during pregnancy, the epithelial cell function is depressed and as a result the degree of keratinization of the gingiva is likely to be decreased. There is also an alteration in collagen metabolism with depressed rates of collagen synthesis.

Estrogen and progesterone, act in the connective tissue inducing fibroblast proliferation and collagen maturation. Non-collagenous connective tissue proteins such as gylcosaminoglycans are more rapidly degraded in tissues with elevated levels of both estrogen and progesterone. Progesterone alters the rate and pattern of collagen production in the gingiva, resulting in reduced repair and maintenance potential, resulting in an altered collagen turnover.[20]

Progesterone increases the permeability of blood vessels in target tissues. The resulting stasis of intravascular cellular flow, the hem-concentration that follows, the transendothelial migration and extra-vascular accumulation of inflammatory cells are all very likely to influence the degree of gingival erythema, edema and hyperplasia seen clinically in some pregnant women. These vascular out-

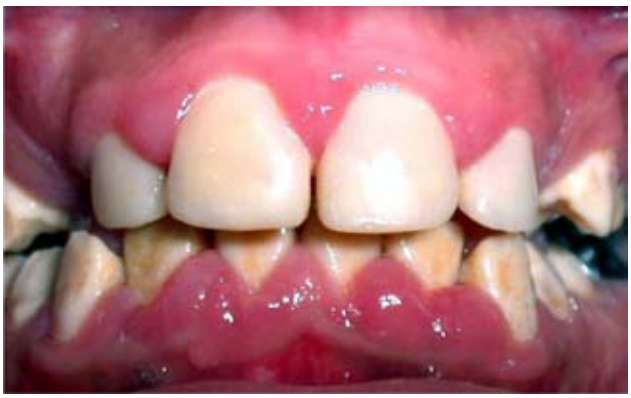

Figure 4. 10 year old female displaying gingival enlargements and potentially hemorrhagic puberty associated gingivitis. Note the severe papillary and marginal erythema and edema characteristic of this disorder. Courtesy Dr. Laura Camacho de Castro. Department of Pediatric Dentistry. Tufts University School of Dental Medicine.

Table IV. Characteristics of puberty-associated gingivitis.[37]

1. Plaque present at gingival margin
2. Pronounced inflammatory response of gingiva
3. Must be circumpubertal as designated by Tanner Stage 2 or greater: (girls, estradiol ≥ 26 pmol/L; boys, testosterone ≥ 8.7 nmol/L)
4. Change in gingival color
5. Change in gingival contour with possible modification of gingival size
6. Increased gingival exudate
7. Bleeding upon provocation
8. Absence of attachment loss
9. Absence of bone loss
10. Reversible following puberty

Table V. Characteristics of menstrual cycle-associated gingivitis.[35]

1. Plaque present at gingival margin
2. Modest inflammatory response of gingiva prior to ovulation.
3. Must be at ovulatory surge when luteininzing hormone levels are > 25 mLU/mL and/or estradiol levels are > 200 pg/mL
4. Increase in gingival exudate by at least 20% during ovulation
5. Absence of attachment loss
6. Absence of bone loss
7. Reversible following ovulation

comes from elevated progesterone levels combined with the heightened epithelial cell, fibroblast, and angioblast proliferation produced by elevated levels of estrogen, complete the pathologic development of exaggerated inflammation and gingival bleeding during pregnancy.[21,22]

The role of sex hormones in the local immune system

The immune response is believed to be depressed during pregnancy so as to allow survival of the fetus as an allograft. Due to the presence of specific sex steroid hormone receptors, particularly progesterone, on imminucompetent cells, the percentages of T lymphocytes bearing CD3 and CD4 markers decreases.[23] Consequently, CD4/CD8 ratios decline and there may be a resulting depression of cell mediated immune response and heightened cytotoxicity.[24] In addition, increased neutrophil chemotaxis, depressed antibody production by B cell lines, and down regulation of IL-6 has been reported during pregnancy.[25,26] That being the case, the pathogenesis of the inflammatory periodontal lesion is probably altered during pregnancy, and these specific immunologic changes will increase the tissue susceptibility to pathogenic bacteria. Progesterone also has a stimulating effect in the production of potent mediators of inflammation such as prostaglandin E2 and complement activating elements of the fibrinolytic system.[27]

Gingival diseases associated with sex steroid hormones

Throughout women's hormonal cycles (puberty, menstruation, pregnancy and menopause), alterations on the periodontal tissues may be easily observed. Bacterial plaque biofilm in combination with steroid hormones will produce exaggerated gingival responses which will develop into complex gingival diseases, which may easily progress into periodontitis if they are not treated adequately and/or on time.

Puberty-associated gingivitis

Female sexual maturation (puberty) is characterized by a series of endocrinological events that produces physical and behavioral changes. The increased production of estradiol and progesterone, during puberty, is associated with an increase in the gingival index[28] an increase in subgingival black-pigmented anaerobic bacteria and an increase in gingival inflammation.[29,30]

The current periodontal disease classification describes Puberty-Associated Gingivitis as having susceptibility towards developing clinical signs of inflammation with relatively small amounts of bacterial plaque present during this period.[31] Gingival inflammation during puberty is not related to increase in plaque levels.[23,33]

The incidence and severity of gingivitis in adolescents are influenced by a variety of factors, includ-

Table VI. Characteristics of pregnancy-associated gingivitis.[35]

1. Plaque present at gingival margin
2. Pronounced inflammatory response of gingiva
3. Onset is in pregnant women (2nd or 3rd trimester)
4. Change in gingival color
5. Change in gingival contour
6. Increase in gingival exudate
7. Bleeding upon provocation
8. Absence of attachment loss
9. Absence of bone loss
10. Reversible at parturition

Table VII. Characteristics of pregnancy-associated pyogenic granuloma (PAPG).[35]

1. Plaque present at gingival margin
2. Pronounced inflammatory response of gingiva
3. Can occur anytime during pregnancy
4. More common in maxilla
5. More common interproximally
6. Sessile or pedunculated protuberant mass
7. Not a neoplasm; has histologic appearance of a pyogenic granuloma
8. Regresses following parturition

ing plaque levels, dental caries, mouth breathing, crowding of the teeth, and tooth eruption.[34] The dramatic increase in steroid hormone levels during puberty has a transitory effect on the inflammatory status of the gingiva.35 This gingivitis manifests as marginal and interdental gingival enlargement, mainly on the facial surfaces.[36] A transient period of enhanced gingival inflammatory response to dental plaque exists during this period of female development and maturation *(Figure 4)*.

With the onset of adulthood, the severity of the gingival reactions will become reduced, but only local debridement of teeth and tissues along with improved oral hygiene will permit complete return to health. The practice of good oral hygiene during puberty keeps puberty gingivitis less of a problem than it could be among adolescent females *(Table IV)*.

Menstrual cycle-associated gingivitis

Once a woman becomes sexually mature her reproductive life is demarcated by the periodic secretion of estrogen and progesterone over 25-30 day periods until menopause. Ordinarily, the menstrual cycle is not associated with corresponding marked gingival changes, and women with a clinically healthy periodontium experience few significant periodontal changes as a result of hormonal fluctuation during menstruation.[12] However, an increase in gingival crevicular fluid by at least 20% has been reported during ovulation in more than 75% of females. In the presence of preexisting gingivitis clinical signs and symptoms of inflammation become exaggerated.[38,39] The highest levels of circulating estradiol and progesterone are found just before ovulation, consistent with the highest levels of gingival inflammation. Other oral lesions in addition to menstrual cycle-associated gingivitis are observed, such as, intraoral recurrent aph-

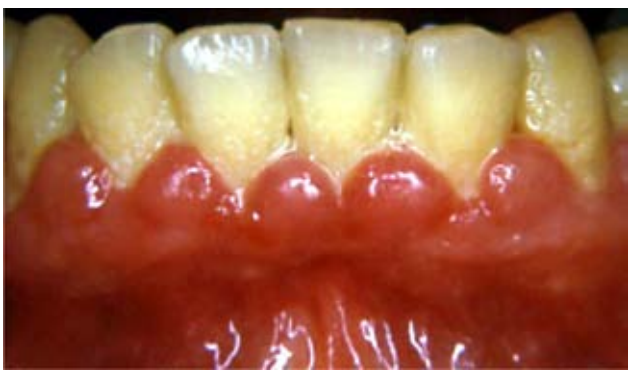

Figure 6. A 19 year old female, in her third trimester of pregnancy displaying severe papillary, marginal, and attached gingival erythema and edema. Note the marked enlargement of the papillary gingival. Plaque biofilm is in abundance. Courtesy Dr Robert Rudy, Department of Periodontology, Tufts University School of Dental Medicine

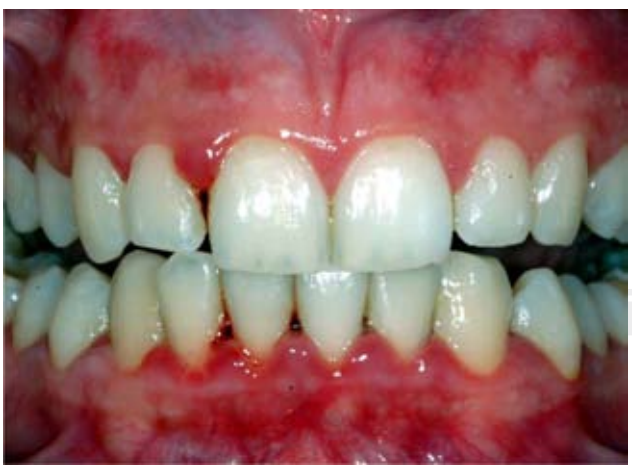

Figure 5. 19 year old female patient during the first week of her menstrual cycle displaying generalized papillary edema and erythema. Note the gingival enlargement and hemorrhagic quality of the severely inflamed gingiva.

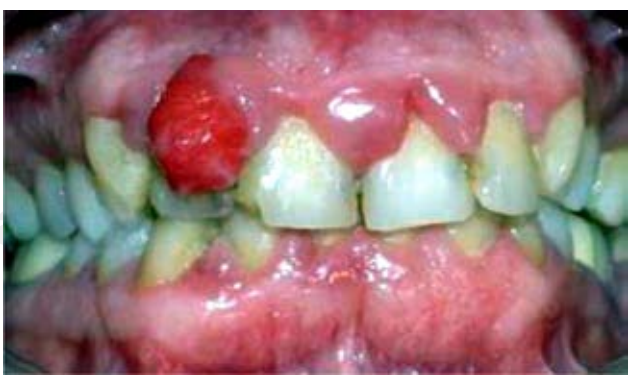

Figure 7. 34 year old 3 months post-partum female displaying severe chronic periodontitis with a residual pregnancy- associated pyogenic granuloma. Courtesy of Dr. Sara Traveria, Departamento de Periodoncia, Universitat Internacional de Catalunya.

thous lesions,[40] herpes labialis lesions and infections with Candida albicans (thrush) have been documented *(Table V and Figure 5)*.[41]

Pregnancy gingivitis

The sustained elevation in plasma hormone levels over the nine months during pregnancy makes pregnancy gingivitis the most distinguishing steroidal sex hormone related oral alteration. The prevalence and severity of gingival inflammation is related to increased production of sex steroid hormones. But this was not always the case as the condition was reported since 1874,[42,43] before there was clear understanding of hormone fluctuations during pregnancy and any impact they may have on the periodontium. It seems now that estrogen and progesterone have a predilection to accumulate in gingival tissues.[44]

Pregnancy itself does not cause gingivitis; rather it only accentuates the typical inflammatory response to the bacterial plaque biofilm during Plaque-Associated Gingivitis. In the absence of bacteria, pregnancy gingivitis does not occur. Pregnancy gingivitis usually becomes apparent in the second and third month of pregnancy, reaching its most severe state in the eighth month, and then it decreases during the 9th month when hormone levels decrease. By one-year post-partum, the gingival tissues will have resumed the character of tissues before pregnancy.[45] The tissues will only return to a state of health after the elimination of the bacterial etiology.

Pregnancy gingivitis affects 30–100% of all pregnant women.[46,47] In its clinical appearance, it is more common in the anterior segment of the mouth with a predilection to the papillary gingiva. Gingival probing depths are deeper, bleeding on probing or tooth brushing is increased and gingival crevicular fluid flow is elevated.[48] Because of the longstanding state of inflammation, the gingiva will often appear discolored and cyanotic with a marked tendency to bleed. When gingivitis or periodontitis are present before pregnancy, the condition has been found to worsen dramatically.[36] The periodontal inflammation and destruction may be increased even more if combined with other systemic alterations such as diabetes *(Table VI and Figure 6)*.

Oral contraceptive-associated gingivitis

Oral contraceptives achieve their desired effect by mimicking pregnancy. As such, they also affect the biology of gingival tissues as typically seen in pregnancy. Indeed, gingival changes that resemble early pregnancy are common in women taking oral contraceptives.[19,49] Because not all oral contraceptives have similar formulations, some may produce a more marked effect on the gingiva than others, but hormone dosage does not seem to correlate with the severity of clinical signs and symptoms of gingivitis.[50] It also appears that the severity of these changes increase with the duration of use of the oral contraceptives.[51] The effects of oral contraceptives on the gingival will always be reversed when the agents are discontinued.

Pregnancy associated pyogenic granuloma (PAPG)

Pregnancy Associated Pyogenic Granuloma (PAPG), also known as pregnancy tumor, epulis angiomatosa, epulis telangiectaticum, lobular capillary hemangioma, granuloma gravidarum, pyogenic granuloma, or Crocker-Hartzell disease is another gingival disease associated with steroidal sex hormone production that can developed as early as the first trimester of pregnancy.[52] PAPG can be seen in the 0.5–9.6% of pregnant women.[48,53] Although not technically a neoplasm, PAPG is frequently described as a localized, discrete, tumor-like mass of gingival enlargement. In reality, PAPG originates as an exaggerated inflammatory response to bacterial plaque and calculus and typically appears as a painless protuberant, mushroom-like, exophytic mass of 1 to 2 cm in size, attached by a sessile or pedunculated base from the gingival margin or more commonly from an interproximal spaces of the maxillary anterior teeth.[40] PAPG commonly displays a discoloration that ranges from red to purplish red to deep blue. PAPG will bleed freely upon gentle manipulation. PAPG cannot be distinguished clinically or histologically from pyogenic granulomas occurring in non-pregnant women. Following parturition, the lesion may regress or completely disappear, and has a tendency to recur if not excised correctly *(Table VII and Figure 7)*.

Menopause and gingival disorders

Changes in oral and periodontal tissues associated with menopause between ages 45-55 and the postmenopausal period are uncommon, but they occur frequently enough to warrant clinical awareness.[35,54] During menopause, or following a total hysterectomy, the rhythmic female cycle of hormone fluctuation of circulating estrogens ceases.[20] As a result, affected women experience an uncommon disorder known as menopausal gingivostomatitis. Symptoms include changes in the oral mucosa that are comparable to those that occur in the vaginal mucosa in the same individual. The oral mucosa and gingiva become dry, pale, erythematous, and bleed easily. Histologically, again similar to atrophic vaginitis, the epithelium becomes thin, atrophic and sometimes ulcerated resembling the desquamative lesions of erosive lichen planus or benign mucous membrane pemphigoid.[31,35] Affected women classically present with oral dry and burning sensation, alterations in taste, and difficulty wearing removable appliances.

Treatment

Traditional treatment of gingival and periodontal diseases involves the reduction/eradication of periodontal pathogens, mainly through mechanical debridement often accompanied with the delivery of local and/or systemic antibiotics, and the biomodification of the host response. Depending on the evidence for persistence and the progression of the disease, surgical therapy will be indicated in order:

1) To create access to perform adequate mechanical instrumentation.
2) To reshape irregular bony and gingival anatomical conditions in order to promote a healthier environment.
3) To facilitate maintenance procedures by both the professional doctor as well as the patient on a daily basis.

After therapy, beneficial and pathogenic species will recolonize. It is the responsibility of the treating dentist and/or periodontist, to instruct their patients on how to take care of themselves on a daily basis, as well as scheduling periodic checkups that vary from 2 to 6 months depending on the degree of destruction, susceptibility, and ability of the patient to care of themselves.

In the case of sex hormone influenced periodontal diseases, as described here, an interdisciplinary approach between the dentist and/or periodontist, and the patients personal treating physician is essential for their successful management.

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