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The Influence of Sex Steroid Hormones on Gingiva of Women

A research:

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بسم الله الرحمن الرحيم

﴿ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ ﴾

صدق الله العلي العظيم

(سورة المجادلة: 11)

Dedication

Our study trip has reached its end after exhaustion and hardship. We are grateful to everyone who has credited and helped our career, our parents, family, friends and doctors and particularly thanks to dr.Ibtisam karim for her support, kind and help us to complete the research and We present to you with great thankful a study of our graduation.

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ABSTRACT

Steroid sex hormones have a significant effect on different organ systems. As far as gingiva are concerned, they can influence the cellular proliferation, differentiation and growth of keratinocytes and fibroblasts. Estrogen is mainly responsible for alterations in blood vessels and progesterone stimulates the production of inflammatory mediators. In addition, some micro- organisms found in the human mouth synthesize enzymes needed for steroid synthesis and catabolism. In women, during puberty, ovulation and pregnancy, there is an increase in the production of sex steroid hormones which results in increased gingival inflammation, characterized by gingival enlargement, increased gingival bleeding and crevicular fluid flow and microbial changes.

Sex steroid hormones (SSH) are cholesterol-derived molecules. They are secreted into saliva and enter the oral cavity, triggering physiological responses from oral tissues, with possible clinical implications, such as gingival inflammation and bleeding. SSH and hormonal changes affect not only oral host cells but also oral microorganisms. Historically, most research has focused on the effect of hormonal changes on specific bacteria and yeasts.

Chapter ONE

Introduction

1.1 Introduction:

Steroid sex hormones are derived from cholesterol and as a common structure they have three rings of six carbon atoms. They are believed to play an important role in the maintenance of the skeletal integrity, including the alveolar bone. The steroid sex hormones, such as estrogen and estradiol have been known for their effect on bone mineral metabolism. Other bone turnover- related hormones include progesterone, testosterone, and dihydrotestosterone, androstenedione and sex hormone-binding globulin.(1)Among these, estrogens, progesterone and androgen (testosterone) have been most linked with periodontal pathogenesis in women, estrogen and progesterone contribute to physiological changes at specific life phases. Puberty, menstrual cycle, pregnancy and menopause are all phases that specifically influence oral and periodontal health in women. Increased hormonal levels during puberty affect gingival tissues and the subgingival microflora.(2) For example, during puberty, Prevotella intermedia and Capnocytophaga bacterial species emerge. (3) Moreover, bleeding may occur when patients masticate or brush their teeth. In addition to puberty-induced changes, gingival tissues are more edematous during the menstrual cycle and erythematous before its onset. Consequently, increased gingival bleeding and exudation (4)has been observed during the menstrual period and is sometimes associated with slight increases in tooth mobility.(5)

Estrogen and progesterone are responsible for physiological changes in women at specific phases of their life, starting in puberty. Estrogen induces several of the pubertal developmental changes in females, and progesterone acts synergistically with estrogen to control the menstrual cycle and to inhibit follitropin secretion by the anterior pituitary gland. (6) Specifically, estrogens can influence the cytodifferentiation of stratified squamous epithelium as well as

the synthesis and maintenance of fibrous collagen.(6) Estrogen receptors found in osteoblast- like cells provide a mechanism for the direct action on bone. These receptors were also located in periosteal fibroblasts, scattered fibroblasts of the lamina propria(7) and periodontal ligament (PDL) .fibroblasts,(8) proving the direct action of sex hormones on different periodontal tissues. The estrogens are a family of hormones synthesized in a variety of tissues. 17ß-Estradiol is the primary estrogen of ovarian origin. In some species, estrone, synthesized in numerous tissues, is more abundant. In pregnancy, relatively more estriol is produced, and this comes from the placenta. The general pathway and the subcellular localization of the enzymes involved in the early steps of estradiol synthesis are the same as those involved in androgen biosynthesis. Features unique to the ovary. are illustrated in Figure 1-1.

Estrogens are formed by the aromatization of androgens in a complex process that involves three hydroxylation steps, each of which requires 02 and NADPH. The aromatase enzyme complex is thought to include a P450 monooxygenase. Estradiol is formed if the substrate of this enzyme complex is testosterone, whereas estrone results**.**

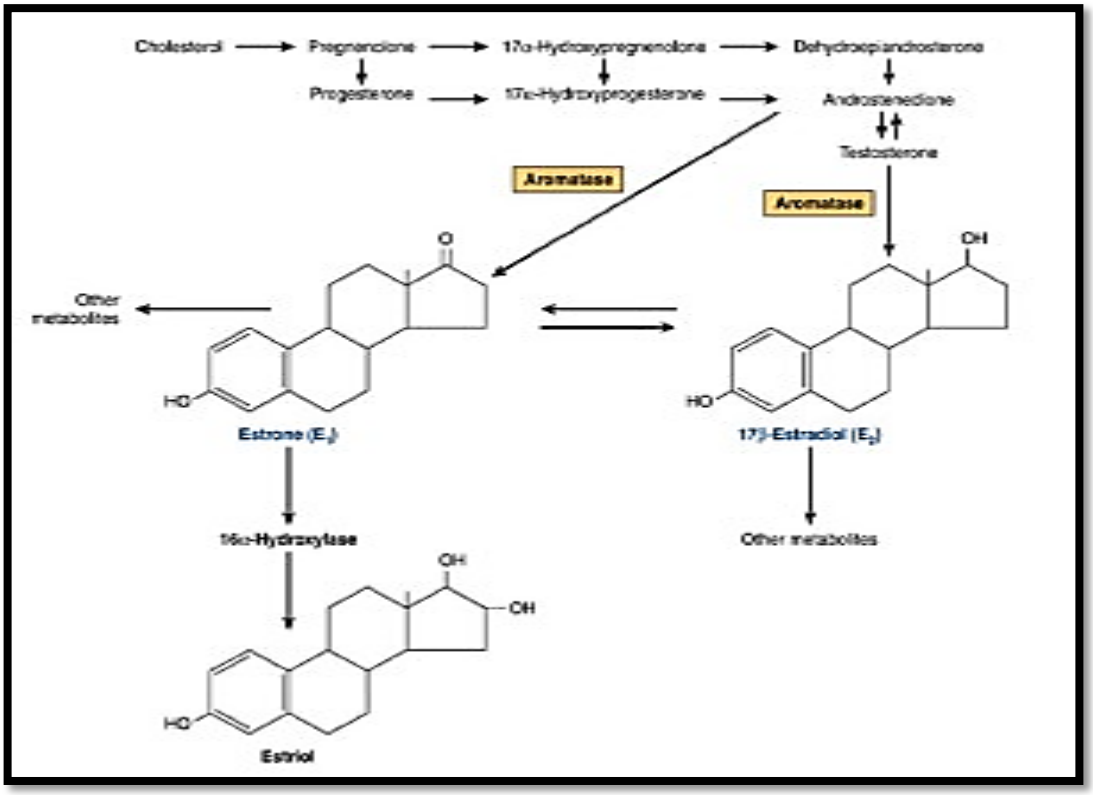


FIGURE 1- 1 Biosynthesis of estrogens. (9)

from the aromatization of androstenedione The cellular source of the various ovarian steroids has been difficult to unravel, but a transfer of substrates between two cell types is involved. Theca cells are the source of androstenedione and testosterone. These are converted by the aromatase enzyme in granulosa cells to estrone and estradiol, respectively. Significant amounts of estrogens are produced by the peripheral aromatization of androgens. In human males, the peripheral aromatization of testosterone to estradiol (E2) accounts for 80% of the production of the latter. In females adrenal androgens are important substrates since as much as 50% of the E2produced during pregnancy comes from the aromatization of androgens. Finally, conversion of androstenedione to estrone is the major source of estrogens in postmenopausal women Progesterone, a precursor for all steroid hormones, is produced and secreted by the corpus luteum as an end product hormone because these cells do not contain the enzymes necessary to convert progesterone to other steroid hormones. (9) (Figure 2-1).

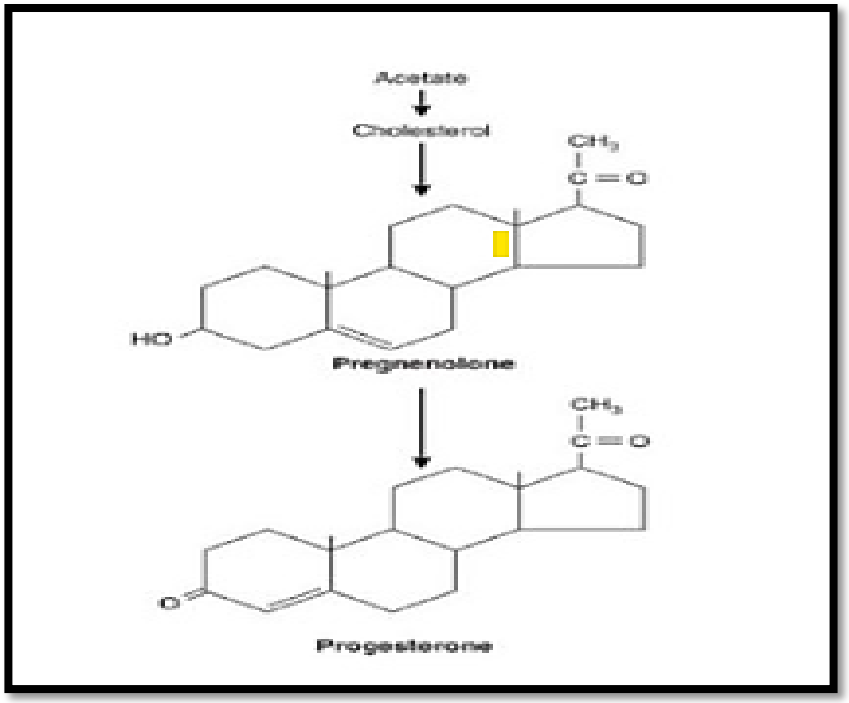


FIGURE 2-1: Biosynthesis of progesterone in the corpus luteum. (9)

1.2 Sex Steroid Hormones as a Balancing Factor in Oral Host Microbiome Interactions:

oral cavity is not exempt from the effect of these molecules (sex steroid hormones). In fact, SSH can diffuse into saliva through capillaries and salivary ducts (10). Consequently, they are capable of reaching intra-oral target tissues such as the gingiva and the periodontium, where they induce a response (11). Likewise, microorganisms present in the oral cavity are exposed to SSH and .(specific oral bacteria and yeast have been shown to be affected by them(12) During pregnancy, the surge in hormonal levels triggers responses by oral tissues, with 30-100% of women undergoing gingival changes such as inflammation and increased bleeding (13). Similar changes have also been observed during physiological and artificially induced hormonal shift periods, as well as an effect on oral bacteria (14) Researchers have tried to explain why oral clinical changes take place, which mechanisms are involved, and the possible implications of both for the host. It has been proposed that SSH are capable of

affecting periodontal tissues and their surrounding environment through four different mechanisms:

(1) by locally influencing proliferation of fibroblasts and epithelial cells؛
(2) by increasing vascular permeability؛
(3) by elevating levels of immune cells in the periodontium; and
(4) by inducing changes in certain oral microorganisms (15).

Studies in females and males on the effects of SSH on oral bacteria and fungi have been inconclusive. Moreover, the study of the oral microbiome, understood as the microorganisms present in the oral cavity, their genetic information and the environment in which they interact (16) has gained interest (17) and represents a gap in our knowledge that needs to be addressed.

1.3 The Interaction Between Oral Microorganisms and Sex Steroid Hormones:

- Who Are They and How Do They React ?

Several oral bacteria and Candida species have been reported to respond to the presence of SSH. SSH-responsive microorganisms have been classified into four groups based on their putative role in oral health and disease and in line with the classification used in the majority of the reviewed literature. These are:

(1) periodontal-disease-associated bacteria؛
(2) caries-associated bacteria؛
(3) oral-health-associated bacteria; and
(4) oral fungi (18).

1.3.1 Periodontal Disease Associated Bacteria:

in the absence of vitamin K(19), two periodontal bacteria - Bacteroides melaninogenicus subsp., intermedius (now Prevotella intermedia), and Bacteroides melaninogenicus subsp. melaninogenicus (now Prevotella melaninogenica) - used estradiol and progesterone as growth factors in the absence of vitamin K (20). They also showed that bacteroides gingivalis (now Porphyromonas gingivalis) and P. intermedia were able to nearly quintuplicate their

SSH uptake when fumarate was added to the medium, significantly enhancing their metabolism.

1.3.2 Caries Associated Bacteria:

Ojanotko Harri et al investigated the metabolism of progesterone and testosterone by Streptococcus mutans strain Ingbritt cultures (21)showed that S. mutans is capable of metabolizing testosterone and progesterone by measuring the presence of metabolites in the culture medium. Based on the previously.

obtained results, the same group published their work on metabolism of 17b- estradiol by oral S. mutans, amongst other microorganisms (22), showing 17b- hydroxysteroid dehydrogenase activity of this bacterium. Together, these publications are the only available evidence that S. mutans is capable of metabolizing SSH in vitro.

1.3.3 Oral Health Associated Bacteria:

The same study that tested the ability of S. mutans to metabolize 17b-estradiol also analyzed the response of S. sanguis (22), which also showed 17b- hydroxysteroid dehydrogenase activity. This is the only available evidence supporting the hypothesis that oral-health-related bacteria are also capable of metabolizing SSH in vitro.

1.3.4 Oral Fungi:

Earlier studies have reported that Candida species possess estrogen (C. albicans and C. glabrata) and progesterone (C. albicans) binding sites (23). Estrogen has been described to stimulate growth in C. albicans, as well as the enhancement of several virulence factors (24). This includes the formation of hyphae (25) and expression of CDR1 and CDR2 (26), important genes in drug resistance. Progesterone is known to alter gene expression, both favoring resistance to drugs (27) as well as impairing the yeast's ability to form biofilms, colonize and invade the host (28) Unfortunately, most of the available evidence on Candida has focused on the development of vaginitis (29) and few reports have explored the role of SSH in the oral cavity and C. albicans behavior (30). This comes to no surprise, since fungi have been systematically excluded from oral environmental studies and little is known about their commensal behavior in contrast to their role in oral pathology (31).

1.4 The effect of SSH on the host :role in immune fitness :

Up until now, only three studies have investigated the effect of SSH on the response of human gingival fibroblasts to oral bacteria in vitro (32). The dynamics between SSH, oral bacteria and other cell types is not known.

In 1995, Soory cultured gingival fibroblasts from healthy gingival tissue in the presence of testosterone and supernatants obtained from bacterial cultures of A. actinomycetemcomitans, P. intermedia and P. gingivalis (33). The presence of these bacterial supernatants increased the .cell's ability to convert testosterone into dihydrotestosterone (DHT). In a later study, gingival fibroblasts from chronically inflamed gingival tissue were cultured in the presence of 4- androstenedione and supernatants from the same bacterial cultures, separately(34). This interaction resulted in an increased conversion rate of 4- androstenedione to testosterone by gingival fibroblasts when grown in the presence of each bacterial culture's supernatant. Yokoyama et al. assessed the reaction of gingival fibroblasts in the presence of C. rectus in combination with estradiol (35). An additive effect was observed in the production of vascular endothelial growth factor (VEGF) by these gingival fibroblasts. VEGF is a potent blood vessel function regulator that affects the endothelium, including the promotion of hyperpermeability, angiogenesis and endothelial cell growth (36)

1.5 Effects of Estrogen on the Periodontal Tissues:

-Decreases keratinization while increasing epithelial glycogen that results in the diminution in the effectiveness of the epithelial barrier(37).

-Increases cellular proliferation in blood vessels(38).

-Stimulates PMNL phagocytosis(39).

-Inhibits PMNL chemotaxis (40).

-Suppress leukocyte production from the bone marrow(41).

-Inhibits proinflammatory cytokins released by human marrow cells(41)?

-Reduces T-cell mediated inflammation(42).

-Stimulates the proliferation of the gingival fibroblasts(41).

-Stimulates the synthesis and maturation of gingival connective tissues(43).

-Increases the amount of gingival inflammation with no increase of plaque.(44).

1.6 Effects of Progesterone on the Periodontal Tissues:

-Increases vascular dilatation, thus increases permeability (45).

-Increases the production of prostaglandins (46).

-Increases PMNL and prostaglandin E2 in the gingival crevicular fluid (GCF)(47) -Reduces glucocorticoid anti-inflammatory effect(48).

-Inhibits collagen and noncollagen synthesis in PDL fibroblast(49).

-Alters rate and pattern of collagen production in gingiva resulting in reduced repair and maintenance potential (50).

-Increases the metabolic breakdown of folate which is necessary for tissue maintenance and repair (51).

Chapter Two

Influence of SSH On Periodontium During different period in female

2.1 Influence On Periodontium During Puberty

Puberty is a complex, integrative, and coordinated transition, marked by change in body, brain, behaviour, cognition, and emotion. (52) And Puberty is the gateway to adult reproductive com- petence, encompassing a suite of changes resulting from maturation of the brain and neuroendocrine function (53). During puberty, there are raised levels of testosterone in males and estradiol in females. Several studies have demonstrated an increase in gingival inflammation in children of circum-pubertal age, with no change in plaque levels (54).

In a longitudinal study, Mombelli et al. (1989) reported that the mean papillary bleeding scores and percentage of interdental bleeding sites correlated with the development of secondary sexual characteristics at puberty, while other studies did not find a significant correlation between the onset of puberty and gingival changes in parapubescent women (55) These discrepancies may be attributed to factors such as the oral hygiene status of the population and study design. The prevalence of certain periodontal pathogens reported during puberty may have a direct association with the hormones present and their utilization by selected pathogens. For example Prevotella intermedia is able to substitute progesterone and estrogen for menadione (vitamin K) as an essential nutrient (56). An association between pubertal gingivitis, Prevotella intermedia and serum levels of testosterone, estrogen and progesterone has been reported in a longitudinal study (57).

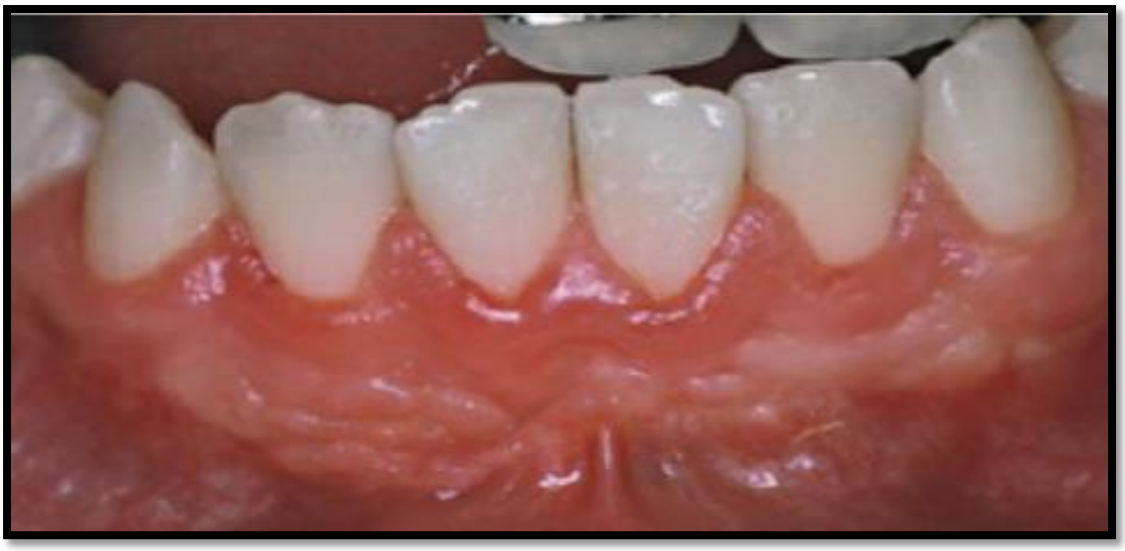


Figure (3-1)Gingivitis during puberty, with edema, discoloration, and enlargement of the entire gingival margin and papillary areas around the .mandibular incisors (58)

2.2 Clinical and microbial changes during puberty include:

- •Increase gingival inflammation without accompanying an increase in plaque levels (59)(60).
- Increased prevalence of certain bacterial species such as Preveotella intermedia and Capnocytophaga species (61).
- Enhanced blood circulation in the end terminal capillary loops and associated increased prevalence of gingivitis/bleeding tendency.(61).

2.3 Puberty gingivitis:

Pubertal gingivitis or steroid hormone-associated gingivitis is described as aggravation of gingivitis by pre-pubertal and pubertal alterations in sex hormone levels. This can be justified by estrogen and progesterone upsurge in the gingival tissues leading to vasodilatation and proliferation and increased susceptibility to inflammation. The interrelationship between elevated levels of the gonadotrophic hormones and pubertal gingivitis is noticeable from the fact that gingival inflammation peaks prior in girls (10-13 years) than in boys (13-15 years). According to in vivo evidence, P. intermedius is associated with the elevated levels of plasma estrogen and progesterone, suggesting that P. intermedius thrives on these hormones for nutrients. It is markedly distinguished by conspicuous inflammation, bluish-red appearances, swelling, and overgrowth, prominent bulbous interproximal papillae of anterior segments which are precipitated from local irritating factors that would normally evoke a relatively benign gingival reaction. Management of puberty gingivitis should be targeted towards professional prophylaxis, elimination of all local irritants, restoration of carious teeth, and nutritional monitoring to ensure a sufficient nutritional status. Occasionally, the fibrotic transformation of the gingival swelling warrants timely surgical debridement. (62)

2.3.1 Management:

During puberty, education of the parent or caregiver is part of successful periodontal therapy. Preventive care, including a vigorous program of oral hygiene, is also vital (63) Milder gingivitis cases respond well to scaling and root planing, with frequent oral hygiene reinforcement. Severe cases of gingivitis may require microbial culturing, antimicrobial mouthwashes and local site delivery, or antibiotic therapy. Periodontal maintenance appointments may need to be more frequent when periodontal instability is identified. The clinician should recognize the periodontal manifestations and intraoral lesions associated with systemic diseases (e.g.,diabetes) (64)(65).

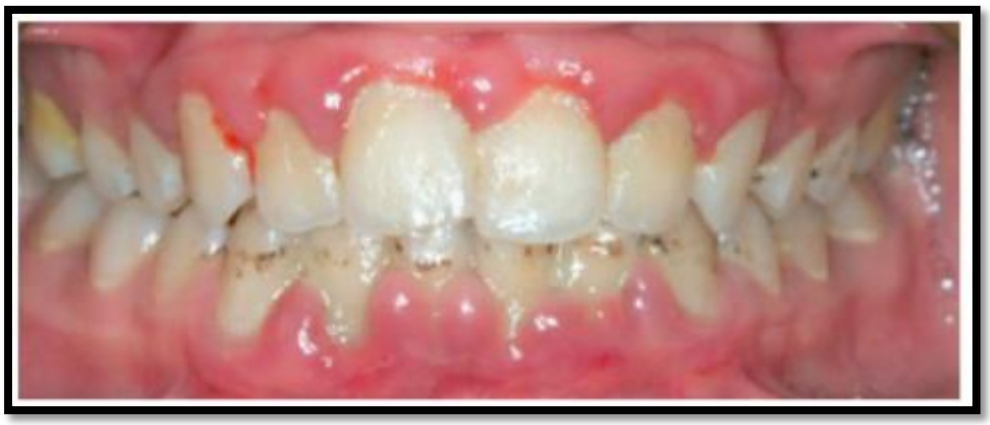


Figure (4-1)Puberty gingivitis in a 14-year-old girl was associated with poor hygiene, crowding of teeth, and mouth breathing. Gingival hyperplasia was confined to the anterior regions (58)

2.4 Influence On Periodontium During Menstruation:

The menstrual cycle is a 25-30-day period, controlled by the secretion of sex hormones, which is responsible for continued ovulation until menopause (66) (67). It can be divided into two phases: a proliferative and a secretory phase, corre- sponding to pre- and post-ovulatory events in the ovaries. The proliferative phase is characterized by a gradual increase in production of gonadotropin (FSH) and of estrogens and, to a lesser degree, progesterone. At ovulation there is. a sudden and marked increase in production of gonadotropin and of estrogens (68) Pre-existing plaque-induced gingivitis may be an important factor in detecting hormone-induced changes during the menstrual cycle. Holm-Pedersen & Loe (1967) demonstrated that women with gingivitis experienced increased inflammation with an associated increase in crevicular fluid exudate during menstruation compared with healthy controls.

Most female patients are not aware of any changes in their gingivae during the menstrual cycle (69), while a few experience enlarged hemorrhagic gingivae in the days preceding menstrual flow. This has been associated with more gingivitis, increased crevicular fluid flow and tooth mobility (70). Early studies demonstrated similar findings during the menstrual cycle in a population with preexisting gingivitis, in response to fluctuations in the levels of estrogen and progesterone (71).

Figure (5-1)Periodic localized color changes of the gingiva around maxillary anterior teeth were associated with menstruation in a 29-year- .old woman (58)

2.5 Clinical Changes in the Periodontal Tissues during Menstruation

- Bleeding and swollen gingiva(72).
- An increase in gingival exudates(73).
- A minor increase in tooth mobility. (72).

2.5.1 Management:

The fluctuating levels of sex hormones during the menstrual cycle induce some changes in the periodontal tissues especially those with pre-existing gingivitis. Conventional non-surgical periodontal therapy is usually the mode of treatment for menstrual gingivitis along with reinforced training of oral hygiene measures. For patients with severe periodontal inflammation and tenderness, the frequency of periodontal recall should be 3-4 months (74).

Some women also experience premenstrual syndrome which consists of various physical and emotional symptoms that may contribute to an exaggerated response to pain. Hence, the clinician may schedule the appointments for periodontal procedures, post menstrual cycle. Other conditions seen during this phase are recurrent aphthous ulcers, increased gag reflex, and other gastrointestinal symptoms. Most of the symptoms are self-limiting and resolves once the cycle begins.

2.6 Influence On Periodontium During Pregnancy:

Periodontal health in pregnant women has become a field of research since the 1960s, resulting in a flurry of studies to focus on it (75). Gingival inflammation associated with pregnancy has been initiated by dental plaque and exacerbated by endogenous steroid hormones (76).

During pregnancy, the increased levels of sex steroid hormones are maintained from the luteal phase which results in implantation of the embryo, until parturition. Pregnant women, near or at term, produce large quantities of estradiol (20 mg/ day), estriol (80 mg/day) and progesterone (300 mg/day). Gingival inflammation initiated by plaque, and exacerbated by these hormonal changes in the second and third trimester of pregnancy, is referred to as pregnancy gingivitis. Parameters such as gingival probing depths (77), bleeding on probing (78) and crevicular fluid flow (79) were found to be increased. These inflammatory features can be minimized by maintaining good plaque control. A more recent study of a rural population of Sri Lankan women (80) showed increased gingivitis of varying degrees of significance amongst all the pregnant women investigated, compared withmatched non-pregnant controls.

There was a progressive increase in inflammation with advancing pregnancy which was more significant in the second and third trimester of pregnancy, despite the plaque levels remaining unchanged. At the third month after parturition, the level of gingival inflammation was similar to that observed in the first trimester of pregnancy. This suggests a direct correlation between gingivitis and sustained, raised levels of gestational hormones during pregnancy, with regression during the postpartum period. In investigations by Cohen et al. (1969) and Tilakaratne et al. (2000a), the values for loss of attachment remained unchanged during pregnancy and three months postpartum.

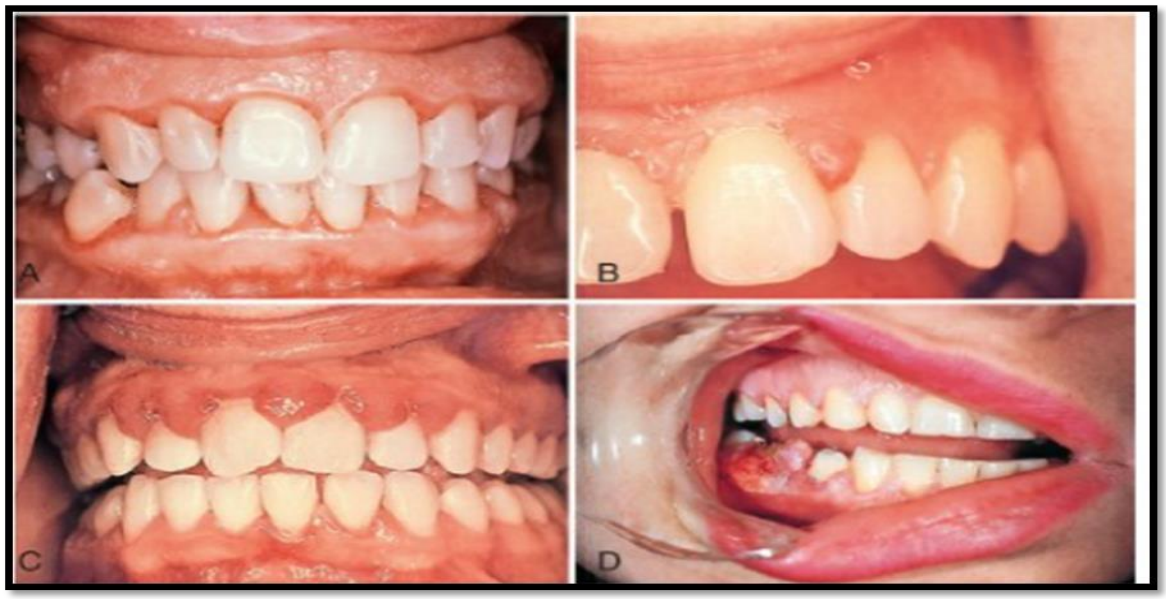


Figure (6-1)Periodontal condition during pregnancy.(58)

- (A)Marginal erythema and easily bleeding gingiva in a woman who is 5 months pregnant.
- (B)Localized incipient gingival enlargement between the maxillary central and lateral incisors in a woman who is 4 months pregnant.
- (C)Generalized gingival enlargement of the interdental papilla and gingival margins on the facial surface of the maxillary incisors in a pregnant woman.
- (D) Extensive gingival, enlargement localized on the buccal surface of the mandibular premolars in a pregnant woman. These ."lesions are often referred to as "pregnancy tumors.

2.7 Pregnancy Related periodontal Changes:

During pregnancy there are specific gingival alterations such as pregnancy gingivitis, characterized by hyper-vascularity and non-specific cellular inflammatory infiltration. Another alteration is the pyogenic granuloma which is an exaggerated proliferative fibrovascular inflammatory reaction located in the gingival

2.7.1 Pregnancy gingivitis:

The development of gingivitis is very frequent, with a reported prevalence of 35% to 100% in pregnancy (81). Pregnancy gingivitis usually develops between the second and eighth month of pregnancy (82). Pregnancy itself does not seemingly cause gingivitis, and a healthy gingival without bacterial challenge usually remains unaffected (83). Periodontitis may be recognized in certain pregnant individuals as a predictive factor for increased risk of having pregnancy complications (84).

Alterations in the immune inflammatory process by hormonal imbalance suggest that estradiol and progesterone are potential determinants responsible for the development of pregnancy gingivitis (85). The levels of serum estradiol and progesterone are elevated throughout the third trimesters of pregnancy, reaching the highest levels during that trimester (86). Interestingly, increased levels of both hormones in saliva have been found associated with the severity of gingival inflammation during pregnancy. Several biological mechanisms have been proposed to explain the pathobiology of the interaction between pregnancy and periodontal disease (87), including increased vascularity and vascular flow, cellular changes, alterations in oral biofilms and depression of the immune system (88) (89) (90). It has c been postulated that the particularly high susceptibility to develop gingival inflammation during pregnancy is associated with qualitative deficiency of maternal immunity, such as decreased function of neutrophils, reduced levels of cytokine production, and impaired function of maternal T lymphocytes. In vitro, several studies show that estradiol and progesterone can have immunosuppressive effects (91). In addition, clinical studies have also demonstrated the biological link between changes in the local cytokine levels and gingival inflammation during pregnancy (92).

Figure(7-1) Moderate form of .pregnancy gingivitis (58)

Figure(7-1) Moderate form of .pregnancy gingivitis (58)B.Figure (8-1)Severe pregnancy gingivitis with hyperplasia can occur in patients with poorly controlled non-insulin-dependent diabetes mellitus. (A) Moderate gingival enlargement. (B) Severe .gingival enlargement (58)

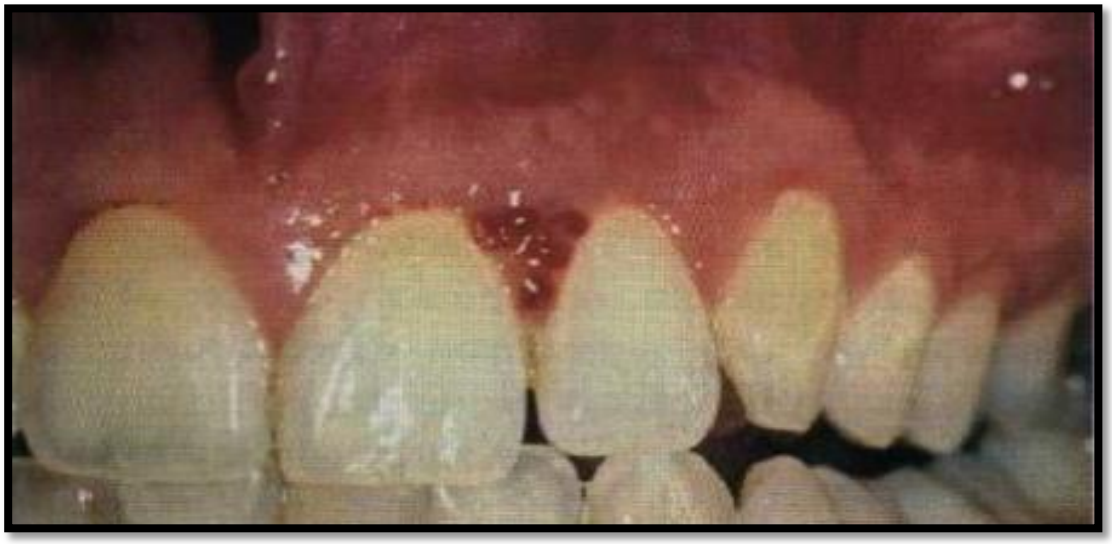
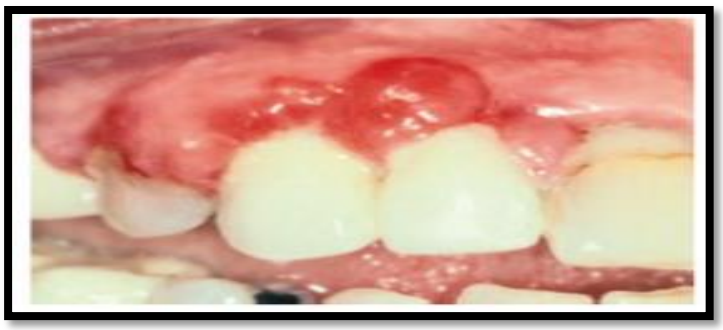


Fig. (9-1) Multilobulated appearance of an early pregnancy epulis, demonstrating vascular elements and tis sue edema

2.7.2 Pyogenic Granuloma:

A pedunculated, fibro-granulomatous lesion can sometimes develop during pregnancy and is referred to as a pregnancy granuloma or epulis. develops only in up to 5% of pregnant women (93). Pyogenic granulomas seem most frequently throughout the second or third month of physiological condition. pyogenic granulomas of pregnancy is usually not associated with alveolar bone loss. Tooth mobility, pocket depth, and gingival fluid are also increased in pregnancy. The levels of sex steroid hormones in saliva increases during pregnancy resulting in alterations in the microbial populations which may contribute to these pathologic changes. When excised the lesions usually do not have a large defect. Afro- American women and women with poor socio-economic status have a significantly increased tendency to develop aggravated
pregnancy-related periodontal changes (94). A combination of the vascular response induced by progesterone and the matrix stimulatory effects of estradiol, contribute to the development of pregnancy granulomas, usually at sites with pre-existing gingivitis (Fig. 9-1). The vascular effects result in a bright red, hyperemic and edematous presentation.



Fig(10-1)Pyogenic granuloma of pregnancy (i.e.pregnancy tumor)

The lesions often occur in the anterior papillae of the maxillary teeth and usually do not exceed 2 cm in diameter. They can bleed when traumatized and their removal is best deferred until after parturition, when there is often considerable regression in their size (95). Surgical removal of the granuloma during pregnancy can result in recurrence due to a combination of poor plaque control and hormone mediated growth of the lesion. Careful oral hygiene and debridement during pregnancy are important in preventing its occurrence (95).

Fig(11-1)Clinical image of pyogenic granuloma in a 27-year-old pregnant .female (58).

2.8 Periodontal treatment during pregnancy:

Pregnant women need to be educated on the consequences of pregnancy on gingival tissues and thoroughly motivated in plaque control measures, with professional treatment as required. They are likely to be more comfortable to receive dental treatment during the second trimester than in the first or third trimester of pregnancy, although emergency treatment is permissible at any stage during pregnancy (96). Since most medications cross the placental barrier and organogenesis occurs mainly in the first trimester, pregnant women are best treated in the second trimester, to avoid the occurrence of developmental defects. Any form of medication during pregnancy must only be used if the gravity of the condition being treated outweighs the consequences. Amongst the antibiotics, tetracycline, vancomycin and streptomycin can contribute to staining of teeth and ototoxic and nephrotoxic effects during 4-9 months of pregnancy; erythromycin, penicillins and cephalosporins are relatively safer, but any medication must only be administered in consultation with the patient's obstetrician (97).

2.9 Menopause and Postmenopaue

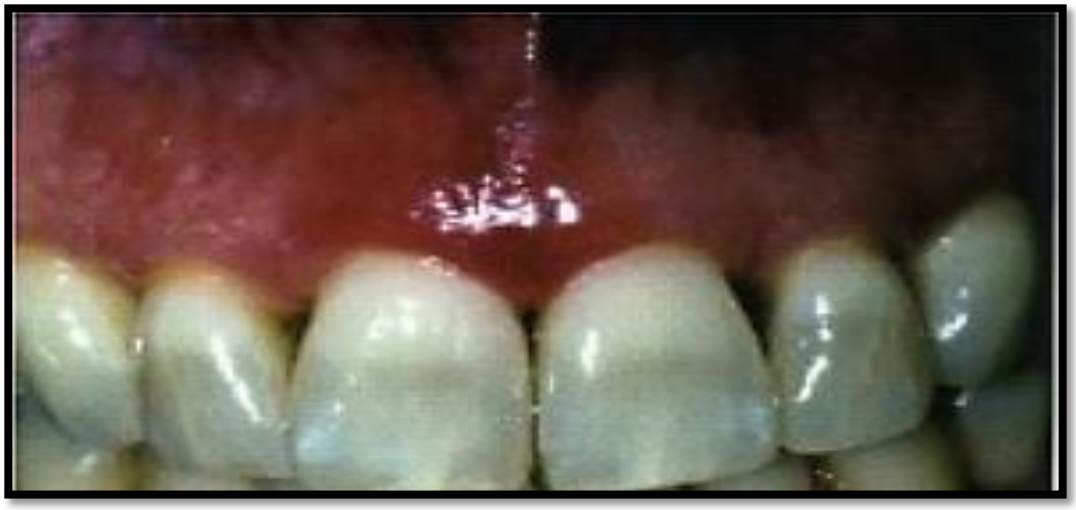
Menopause usually begins between 45 and 55 years of age unless accelerated by hysterectomy and/or ovariectomy(98) The levels of estrogen begin to drop mainly during the late follicular and luteal phase of the menstrual cycle when women approach menopause.(99) Katz and Epstein(100) suggested that peripheral conversion of androgens to estrogens might be the main factor for protecting bone since estrogens have inhibitory effects on osteoclastic functions. The postmenopausal period is associated with an increased risk of osteoporotic fractures, myocardial infarction, menstrual cycle disorders, hot flushes, night sweats, vaginal dryness and possibly with an early onset of Alzheimer’s disease.(101) The most significant problem that develops during menopause is osteoporosis.(98)

2.10 Clinical Changes in the Periodontal Tissues during Menopause and Postmenopause:

-Reduction in epithelial keratinization(102)
-A reduction in salivary gland flow (103)
-Drying of the oral tissues(104)
-Redness and abnormal paleness of the gingival tissues(104)
-Bleeding on probing and brushing.(104)

2.11 Menopause and osteoporosis

During menopause there is a decline in hormonal levels due to decreased ovarian function. This is characterized by tissue changes such as desquamation of gingival epithelium (Fig.12-1) and osteoporosis . which may be attributed to hormone deficiency. It has been demonstrated that women with early onset of menopause have a higher incidence of osteoporosis and significantly lower bone mineral density (105). A third of women over age 60 are affected by postmenopausal osteoporosis (106). The changes involved are a reduction in bone density, affecting its mass and strength without significantly affecting its chemical composition. An alteration in the calciumphosphate equilibrium due to deficient absorption of dietary calcium and increased excretion due to diminished estrogen levels can account for some of the bone changes seen in postmenopausal women (107), usually involving the mandible more than the maxilla Estrogen replacement therapy has been shown to prevent osteoporosis and maintain bone mineral content at several sites throughout the skeleton (108), with a 5% increase in bone mineral content in the region of the head compared to those taking placebo (109). The influence of estrogen on bone mineral density has been demonstrated in these studies, but a cause and effect relationship with periodontal disease is less clear.



Fig(12-1)Clinical appearance of anterior maxillary gingiva with pronounced desquamation in a woman during menopause.

2.12 Contraceptives:

Hormonal contraceptives induce a hormonal condition that stimulates a state of pregnancy to prevent ovulation by the use of gestational hormones. Oral contraceptive agents are one of the most commonly used classes of drugs. The most commonly used contraceptives nowadays consist of low doses of estrogens (30 mg/day) and/or progestins (1.5 mg/day).(110) (111) The influence of contraceptives on the periodontium is not limited to increases in inflammation and in the amount of gingival exudates. (112) These drugs have also been associated with an increase in the prevalence of dry socket after dental extraction,(113) and accelerated progression of periodontal disease (higher gingival index scores and more loss of attachment) when they are used long-term. In contrast, some authors have found no significant influences on the periodontal clinical parameters when comparing oral contraceptives to nonmedicated control groups. (114) .

2.12.1 Management

The medical history should include oral contraceptives along with other medications, and a discussion should include questions regarding oral contraceptives with women of childbearing age. The patient should be informed of the oral and periodontal side effects of oral contraceptives and the need for meticulous home care and compliance with periodontal maintenance. Treatment of gingival inflammation exaggerated by oral contraceptives should include establishing an oral hygiene program and eliminating local predisposing factors. Periodontal surgery may be indicated if resolution after initial therapy (i.e., scaling and root planing) is inadequate. It may be advisable to perform extraction of teeth (especially third molars) on nonestrogenic days of the OC cycle (i.e., days 23 to 28) to reduce the risk of a postoperative localized osteitis(115) however, evidence of this association is inconclusive and warrants further investigation

Conclusion:

The anterior pituitary gland, at the time of puberty, begins secreting gonadotropins: follicle-stimulating hormones and the luteinizing hormone, which act on the ovaries to begin cyclical production and secretion of the two main female sex hormones: estrogen and progesterone The complexities of the female patient are unique to each phase of her life. Female sex hormones play a crucial role, and their cyclic nature is often reflected on the periodontal structures. every patient differs, the dental professional should have sound knowledge and understand-ing of the mechanisms involved that link periodontal dis-ease and female hormone fluctuations. These alterations in the levels of the hormones usually aggravate a preexisting gingival or periodontal condition. Thus, it becomes important to educate patients about these changes and reinforce proper oral hygiene and maintenance. The management of female patients during various stages of life varies from individual to individual. Patient education, prevention, and oral hygiene care and maintenance form the basis of treating female patients.

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18. Sex Steroid Hormones as a Balancing Factor in Oral Host Microbiome Interactions Pilar Cornejo Ulloa, Bastiaan P. Krom and Monique H. van der Veen* Department of Preventive Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and VU University Amsterdam, Amsterdam, Netherlands September 2021 | Volume 11 I
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