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Review Article

Periodontium in females - A review

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ABSTRACT

Periodontium is physically and anatomically similar for both males and females. However, the response of periodontal tissues to hormones varies in both, due to different hormonal interaction.
At different life stages of a female such as puberty, menstruation, pregnancy, menopause and post-menopause, use of contraceptives and hormone replacement therapies; sex hormones like estrogen and progesteron effects periodontal tissues.
Sex hormones play significant roles in modulating the periodontal tissue responses, which can be minimized with good plaque control and with hormone replacement.

1. Introduction

According to the recent classification scheme for periodontal and peri-implant diseases and conditions conducted jointly by the American Acadamy of Periodontology and European Federation of Periodontology, Other conditions affecting the periodontium includes Systemic diseases and conditions, including effect of hormones on periodontium.[1]

At different life stages of a female such as puberty, menstruation, pregnancy, menopause and post-menopause, use of contraceptives and hormone replacement therapies; sex hormones like estrogen and progesteron effects periodontal tissues, bone turnover rate, wound healing and periodontal disease progression. Sex hormones are steroid, derived from cholesterol having three rings of six carbon atoms. They play significant roles in modulating the periodontal tissue responses, which can be minimized with good plaque control and with hormone replacement.

The Bacterial plaque is the primary etiologic factor for initiation of periodontal disease.[2] Sex hormones act as important modifying factors that influence the pathogenesis of periodontal diseases.[3–6] Despite profound research linking periodontal condition with sex hormones kinetics, more definitive molecular mechanisms and therapy still remain to be determined.

They are believed to play an important role in the maintenance of the skeletal integrity, including the alveolar bone. Estrogen and estradiol effect bone mineral metabolism. Other bone turnover-related hormones are progesterone, testosterone and sex hormone-binding globulin. Among these, estrogens, progesterone, and testosterone have been most linked with periodontal pathogenesis.[3]

Effect of Sex Hormone on the periodontium depend on the following 3 factors- gender, age and hormone supplements.

1. Gender: Women are affected more than men (e.g. osteoporosis) when comparing the bone density changes. Lau et al. (2001) reported higher frequency of osteoporotic changes and hip fractures in females compared to males.[7]

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2. Age: Females are affected more as with increasing age and changes in biological cycle like puberty, menstrual cycle, pregnancy, menopause, and oral contraceptive.

1.1. Puberty

Process of sexual maturation resulting in an individual capable of reproduction.[3,8] Changes in physical appearance and behavior,[9–11] related with increased levels of the sex hormones, testosterone in males and estradiol in females.

Changes seen in hormone level during puberty, leads to increases, that remains constant for the entire normal reproductive period. Increased prevalence of gingivitis followed by remission is observed that is not necessarily associated with an increase in the amount of dental plaque.[3,12] Alteration in sub gingival microflora is also seen with increase in the bacterial counts, and prevalence of Prevotella intermedia (Pi) and Capnocytophaga species.[3,13,14] Pi has the ability to substitute estrogen and progesterone for menadione (vitamin K) as an essential growth factor.[15] Capnocytophaga species have been associated with the increased bleeding tendency.[3,14]

Clinical and microbial changes in the periodontal tissues during puberty- Increased gingival inflammation without accompanying increase in plaque levels. Increased prevalence of certain bacterial species such as P.intermedia and Capnocytophaga species.[4]

1.2. Menstrual cycle

Last over a 25-30-day period and is responsible for continued ovulation until menopause.[3,16] In humans, the menstrual cycle is divided into two phases: a follicular or proliferative phase, and a luteal or secretory phase. During the first phase, there is an increase in estrogen levels. At the same time, the luteinizing hormone stimulates progesterone secretion and ovulation. After ovulation, the luteal phase is characterized by an increase in progesterone and estrogen secretion. At the end if fertilization does not occurred, the plasma levels of progesterone and estradiol decline because of the demise of the corpus luteum. Generally, no changes are evident in the periodontium, two different clinical findings have been observed in the oral cavity: gingival bleeding and increased production of gingival exudate.[3,17]

Clinical changes in the periodontal tissues during menstruation - Bleeding and swollen gingival, an increase in gingival exudates, and increase in tooth mobility.[4]

2. Pregnancy

During pregnancy, both progesterone and estrogen are elevated due to continuous production of these hormones by the corpus luteum. By the end of the third trimester, progesterone and estrogen reach peak plasma levels of 100 and 6 ng/ml, respectively, which represent 10 and 30 times the levels observed during the menstrual cycle.

Susceptibility to infections (e.g. periodontal infection) increases during early gestation due to alterations in the immune system[3,18] and can be explained by the hormonal changes observed during pregnancy,[19] suppression on T-cell activity, decreased neutrophil chemotaxis and phagocytosis, altered lymphocyte response and depressed antibody production,[19] chronic maternal stress, and even nutritional deficiency associated with increased nutritional demand by both the mother and the fetus. These immunologic changes are also responsible for periodontal pathologic conditions observed during pregnancy with increase in the gingival crevicular fluid of pregnant women, a situation that is positively correlated with the severity of pregnancy gingivitis.[3]

Clinical and microbial changes in the periodontal tissues during pregnancy - Increased gingival probing depths, increased gingival inflammation, increased gingival crevicular fluid flow, increased bleeding on probing, increased tooth mobility, increased incidences of pyogenic granulomas, increased numbers of periodontopathogens especially P. gingivalis & P.intermedia.[4]

Robinson & Amar (1992) reviewed the influence of pregnancy on the oral cavity and described 4 oral pathological conditions that included a) Pregnancy gingivitis, b) pregnancy granuloma, c) periodontitis and d) dental caries.

2.1. Pregnancy Gingivitis

In 1877, Pinard recorded the first case of "pregnancy gingivitis". Epidemiological studies of pregnancy gingivitis showed a prevalence ranging from 35% (Hasson 1966) to 100% (Lundgren et al 1973). It is characterized by erythema, edema, hyperplasia, and increased bleeding. Histologically the description is the same as gingivitis. The anterior region of the mouth is affected more often, and interproximal sites tend to be more involved (De Liefde 1984).

Increased tissue edema leads to increased pocket depths and relate to transient tooth mobility. Anterior site inflammation may be exacerbated by increase in mouth breathing because of pregnancy rhinitis.

In a study of 130 pregnant women, Machuca et al. (1999) demonstrated gingivitis in 68% of the population, ranging from 46% in technical executives to 88% in manual workers. Cross-sectional studies examining pregnant and postpartum women have shown that pregnancy is associated with significantly more gingivitis than at postpartum, despite similar plaque scores (Silness & Loe 1963). A more recent study of a rural population of Sri Lankan women (Tilakaratne et al. 2000) showed increased gingivitis of varying degrees of significance amongst all the pregnant women investigated, compared with matched 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. (2000) the values for loss of attachment remained unchanged during pregnancy and three months postpartum.

2.2. Pregnancy granuloma/Pregnancy tumor/ and epulis gravidarum

A pregnancy tumour is an pedunculated, sessile fibro-granulomatous lesion which sometimes develop during pregnancy. 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. 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 (Wang et al. 1997). 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. (Wang et al. 1997)

Laser surgical excision of the lesion is recommended, as opposed to scalpel, for less postsurgical bleeding (Pick et al 1987). Surgical removal is usually performed after parturition. However, if the lesion causes functional problems or appears to have deleterious effects on the adjacent periodontium, it can be safely removed under local anesthesia throughout a normal pregnancy, preferably during the second trimester.

Preterm birth, defined as delivery at fewer than 37 weeks gestation, is the most common cause of infant morbidity and mortality among infants. Preterm birth is responsible for 75% of neonatal mortality and 50% of long-term disability in children.[20,21] Various factors have been associated with the delivery of preterm and/or low birth weight infants.

In the recent years the role of infection is receiving attention as a risk factor for preterm deliveries. The etiological role of maternal infection either in the genital tract or elsewhere in the body on preterm delivery remains controversial. But PLBW may be an indirect effect of infection as a consequence of the production of increased level of inflammatory mediators, which shorten gestational age. Offenbacher et al.[22] reported a potential association between maternal periodontal infection and delivery of a preterm low birth weight infant. In a case-control study of 124 pregnant women, women who delivered at less than 37 weeks gestation or an infant weighing less than 2500 g had significantly worse periodontal infection than control women. The mechanism of periodontal disease association with preterm birth is not clear, but likely involves maternal and fetal inflammatory and immune response to the infectious burden. Maternal periodontal disease is association with a maternal inflammatory response, particularly among African-American women.[23] Fetal exposure to oral pathogens occurs,[24] and increases risk for preterm birth. This risk is even higher if there is also a fetal inflammatory response.[25] The mechanism may also involve translocation of oral bacteria to the amniotic cavity, and subsequent placental, uterine, or fetal responses that initiate preterm birth.[26] Despite the lack of reduction in preterm birth, it is important to consider that treatment of maternal periodontal disease during pregnancy is not associated with any adverse maternal or fetal outcomes. In addition, the majority of treatment trials demonstrate that maternal oral health improves with antepartum periodontal therapy,[27–29] a finding that is important for overall maternal health and well-being.

Table 1: Effects of estrogen on the periodontaltissues[5]

1.	Decreases keratinization while increasing epithelial glycogen that results in the diminution in the effectiveness of the epithelial barrier
2.	Increases cellular proliferation in blood vessels
3.	Stimulates neutrophil (PMNL) phagocytosis
4.	Inhibits PMNL chemotaxis
5.	Suppress leukocyte production from the bone marrow
6.	Inhibits proinflammatory cytokins released by human marrow cells
7.	Reduces T-cell mediated inflammation
8.	Stimulates the proliferation of the gingival fibroblasts
9.	Stimulates the synthesis and maturation of gingival connective tissues
10	Increases the amount of gingival inflammation with no increase of plaque

3. Menopause and postmenopause

In women, the principal circulating estrogen is 17b-estradiol. As women approach menopause, the levels of estrogen begin to drop mainly during the late follicular and luteal phase of the menstrual cycle.[30] As a result of this physiologic situation, irregular cycles start to occur. Frequently, the time frame between regular cycles and the cessation of menstrual periods, called perimenopausal transition, is 2-7 years. During this period, the concentration of circulating estrogen decreases while follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentrations increase. Consequently, the effects of estrogen are reduced, therefore compromising

Table 2: Effects of progesterone on the periodontal tissues[5]

1.	Increases vascular dilatation, thus increases permeability
2.	Increases the production of prostaglandins
3.	Increases PMNL and prostaglandin E2 in the gingival crevicular fluid (GCF)
4.	Reduces glucocorticoid anti-inflammatory effect
5.	Inhibits collagen and noncollagen synthesis in PDL fibroblast
6.	Inhibits proliferation of human gingival fibroblast proliferation
7.	Alters rate and pattern of collagen production in gingiva resulting in reduced repair and maintenance potential
8.	Increases the metabolic breakdown of folate which is necessary for tissue maintenance and repair

the anti-inflammatory effect of this hormone on the periodontium.[3] Progesterone is another sex hormone that may play an important role in bone metabolism during pre- and post menopause.[31] It is believed that ovarian deficiency and associated alterations, but not aging, are the predominant causes of bone loss during the first two decades after menopause. Progesterone may compete with glucocorticoids for an osteoblast receptor and inhibit the glucocorticoid-induced osteoporosis. Therefore, postmenopausal bone density reduction may be the result of a combination of the inhibition of osteoclast downregulation by reduced estrogen and the increased cortisol inhibition of osteoblasts via the reduction of competition with progesterone.[5]

Clinical changes in the periodontal tissues during menopause and postmenopause- reduction in epithelial keratinization, reduction in salivary gland flow, drying of the oral tissues, redness and abnormal paleness of the gingival tissues, bleeding on probing and brushing.[5]

3.1. Hormone replacement

Females experience hormonal changes under both physiological (e.g. menstrual cycle, pregnancy) and nonphysiological conditions (e.g. hormone therapy, use of oral contraceptives).

3.2. Contraceptives

The influence of contraceptives on the periodontium is increases in inflammation and in the amount of gingival exudates, increase in the prevalence of dry socket after dental extraction, and accelerated progression of periodontal disease (higher gingival index scores and more loss of attachment).[4]

Impact of contraceptives on clinical and microbial features of periodontal tissues - inflammation ranges from mild edema and erythema to severe inflammation with hemorrhagic or hyperplastic gingival tissue, 50 per cent increase in gingival fluid volume, 16-fold-increase in Bacteroides species.[5]

3.3. Hormone replacement therapy (HRT in postmenopausal women

Estrogen deficiency is the dominant pathogenic factor for osteoporosis in women.[32] Although hormonal replacement in an adequate dosage can slow or prevent bone loss,[33] only a small percentage of postmenopausal women receive such therapy, and many who do fail to comply with the prescribed regimen because of the fear of cancer, irregular bleeding, and other minor side effects. Progesterone alone is not effective in preventing postmenopausal bone and tooth loss[35], but when combined with estrogen it is believed to uncouple formation and resorption to diminish bone resorption induced by estrogen.

Clinical changes in the periodontal tissues during menopause and postmenopause- reduction in epithelial keratinization, reduction in salivary gland flow, drying of the oral tissues, redness and abnormal paleness of the gingival tissues, bleeding on probing and brushing.[5]

Effects of HRT on the periodontal tissues- protection against tooth loss, reduction in gingival bleeding, reduction in the risk of edentulousim.[5]

Hormonal influences on the microbiota- The effects of sex hormones on the subgingival microbiota during pregnancy have been well documented. Kornman & Loesche[34] reported that during the second trimester, plaque levels remained constant, yet gingivitis and gingival bleeding were shown to increase in severity.[35] At the same time, the ratio of subgingival bacterial anaerobes-to-aerobes increased, as well as proportions of Bacteroides melaninogenicus and P. intermedia (2.2-10.1%). Subgingival plaque samples from these patients during the second trimester demonstrated a significantly higher accumulation of estradiol and progesterone than plaque samples at other time periods. Subsequently, both estradiol and progesterone were shown to be selectively accumulated by P. intermedia as a substitute for vitamin K, and thus postulated to be acting as a growth factor for this microorganism.

Not all studies have corroborated these findings, and Jonsson et al.[36] found no difference in levels of P. intermedia at any time during pregnancy or between pregnant and nonpregnant controls in a cross-sectional assessment. This has led to speculation that the increase in P. intermedia seen during the second trimester of pregnancy may actually be independent of estrogens or progesterone and may occur for other reasons. Mariotti[3] has made observations in this regard. First, P. intermedia is seen to increase during the second trimester of pregnancy followed by a decline to postpartum values during the third trimester, despite highly elevated hormone levels still present during the third trimester. Additionally, there was no analysis of

competitive inhibition with other steroid-like molecules performed in the heretofore cited studies; therefore, it is open to question whether the accumulation of estradiol or progesterone in second trimester plaque samples or pure cultures of P. intermedia was sex steroid hormone specific or merely dependent on the lipophilic nature of the plaque sample.[35]

Hormonal influences on the gingival vasculature- the effects of estrogens and progestins on the gingival vasculature could potentially explain the increased edema, erythema, gingival crevicular exudate, and hemorrhagic gingival tissues noted during pregnancy as well as other stages of the reproductive cycle. An increase in gingival crevicular fluid flow has been correlated to elevated sex steroid levels, which indicates that these hormones may affect vascular permeability in the gingival sulcus.[35]

Hormonal influences on cells of the periodontium- the effects of sex hormones on individual cells of the periodontium may also play a significant role in the exaggerated gingival responses seen during the female reproductive cycle and pregnancy. Sex steroid hormones have been shown to directly and indirectly exert influence on cellular proliferation, differentiation, and growth in target tissues, including keratinocytes and fibroblasts in the gingiva.[3] Two theories for the actions of the hormones on these cells involve the role hormones may play in altering the effectiveness of the epithelial barrier to bacterial insult, and in affecting collagen maintenance and repair. Estrogens stimulate epithelial proliferation and increase keratinization of the vaginal mucosa.[6] Some evidence also exists that sex hormones may have a similar effect on the oral mucosal and gingival epithelia, and a reduction in the keratinization of gingival epithelium of postmenopausal women has been shown to accompany declining plasma estrogen levels. Fibroblast proliferation and collagen maturation in gingival connective tissues may be affected by both estrogen and progesterone. By altering collagen turnover, estrogens may stimulate the proliferation of gingival fibroblasts, and the synthesis and maturation of gingival connective tissues. Sex hormones have also been shown to increase the rate of folate metabolism in oral mucosa.[37] Since folate is required for tissue maintenance, increased metabolism could deplete folate stores and inhibit tissue repair. Additionally, progesterone in concentrations corresponding to the third trimester of pregnancy has been shown to lower the synthesis of glycosaminoglycans, a major constituent of the connective tissue matrix of gingiva.[35]

Influence of Sex Hormones on Periodontal/Implant Wound Healing- at a molecular level, research has also shown that sex hormones have a regulatory effect on growth factors involved in the wound healing such as the keratinocyte growth factor,[38] which has been known to have wound healing regulatory effect including stimulation of proliferation, migration, and morphogenesis of pluripotential cells. However, the influence of sex hormones on periodontal wound healing is still largely unknown.[3]

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None.

5. Conflicts of Interest

All contributing authors declare no conflict of interest.

References

1. Caton JG, Armitage G, Berglundh T, Chapple ILC, Jepsen S, Kornman KS, et al. A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. *J Clin Periodontol*. 2018;45(20):S1–S8. doi:10.1111/jcpe.12935.
2. Löe H, Theilade E, Jensen SB. Experimental Gingivitis in Man. *J Periodontol*. 1965;36(3):177–87. doi:10.1902/jop.1965.36.3.177.
3. Mariotti A. Sex Steroid Hormones and Cell Dynamics in the Periodontium. *Crit Rev Oral Biol Med*. 1994;5(1):27–53. doi:10.1177/10454411940050010201.
4. Mascarenhas P, Gapski R, Al-Shammari K, Wang HL. Influence of sex hormones on the periodontium. *J Clin Periodontol*. 2003;30(8):671–81. doi:10.1034/j.1600-051x.2003.00055.x.
5. Güncü GN, Tözüm TF, Çaglayan F. Effects of endogenous sex hormones on the periodontium — Review of literature. *Aust Dent J*. 2005;50(3):138–45. doi:10.1111/j.1834-7819.2005.tb00352.x.
6. Amar SN, Chung KM. Influence of hormonal variation on the periodontium in women. *Periodontology*. 20001994;6:79–87.
7. Lau EM, Suriwongpaisal P, Lee JK, De SD, Festin MR, Saw SM, et al. Risk Factors for Hip Fracture in Asian Men and Women: The Asian Osteoporosis Study. *J Bone Miner Res*. 2001;16(3):572–80. doi:10.1359/jbmr.2001.16.3.572.
8. Ford JJ, D'Occhio MJ. Differentiation of Sexual Behavior in Cattle, Sheep and Swine. *J Animal Sci*. 1989;67(7):1816–23. doi:10.2527/jas1989.6771816x.
9. Buchanan CM, Eccles JS, Becker JB. Are adolescents the victims of raging hormones? Evidence for activational effects of hormones on moods and behavior at adolescence. *Psychol Bull*. 1992;111(1):62–107. doi:10.1037/0033-2909.111.1.62.
10. Angold A. Puberty onset of gender differences in rates of depression: a developmental, epidemiologic and neuroendocrine perspective. *J Affect Disord*. 1993;29(2-3):145–58. doi:10.1016/0165-0327(93)90029-j.
11. Angold A, Costello EJ, Erkanli A, Worthman CM. Pubertal changes in hormone levels and depression in girls. *Psychol Med*. 1999;29(5):1043–53. doi:10.1017/s0033291799008946.
12. Sutcliffe P. A longitudinal study of gingivitis and puberty. *J Periodontal Res*. 1972;7(1):52–8. doi:10.1111/j.1600-0765.1972.tb00631.x.
13. Yanove L, Ellen RP. A clinical and microbiologic examination of gingival disease in parapubescent females. *J Periodontol*. 1986;57:562–7.
14. Gusberti FA, Mombelli A, Lang NP, Minder CE. Changes in subgingival microbiota during puberty. A 4-year longitudinal study. *J Clin Periodontol*. 1990;17(10):685–92. doi:10.1111/j.1600-051x.1990.tb01054.x.
15. Kornman KS, Loesche WJ. Effects of estradiol and progesterone on Bacteroides melaninogenicus and Bacteroides gingivalis. *Infect Immun*. 1982;35(1):256–63. doi:10.1128/iai.35.1.256-263.1982.
16. McCartney CR, Gingrich MB, Hu Y, Evans WS, Marshall JC. Hypothalamic Regulation of Cyclic Ovulation: Evidence That the Increase in Gonadotropin-Releasing Hormone Pulse Frequency during the Follicular Phase Reflects the Gradual Loss of the Restraining Effects of Progesterone. *J Clin Endocrinol Metab*. 2002;87(5):2194–

200. doi:10.1210/jcem.87.5.8484.
17. Grodstein F, Colditz G, Stampfer M. Postmenopausal hormone use and tooth loss: a prospective study. *J Am Dent Assoc*. 1996;127(3):370–7. doi:10.14219/jada.archive.1996.0208.
18. Brabin BJ. Epidemiology of Infection in Pregnancy. *Rev Infect Dis*. 1985;7(5):579–603. doi:10.1093/clinids/7.5.579.
19. Hansen PJ. Regulation of uterine immune function by progesterone-lessons from the sheep. *J Reprod Immunol*. 1998;40:63–79.
20. Markestad T, Kaaresen P, Rønnestad A. Early Death, Morbidity, and Need of Treatment Among Extremely Premature Infants. *Pediatrics*. 2005;115(5):1289–98. doi:10.1542/peds.2004-1482.
21. Mathews TJ, Macdorman MF. Infant mortality statistics from the 2005 period linked birth/infant death set. *Natl Vital Stat Rep*. 2008;57:1–32.
22. Offenbacher S, Katz V, Fertik G. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol*. 1996;67(10):1103–13.
23. Horton AL, Boggess KA, Moss KL, Jared HL, Beck J, Offenbacher S, et al. Periodontal Disease Early in Pregnancy Is Associated With Maternal Systemic Inflammation Among African American Women. *J Periodontol* . 2008;79(7):1127–32. doi:10.1902/jop.2008.070655.
24. Boggess KA, Moss K, Madianos P, Murtha AP, Beck J, Offenbacher S, et al. Fetal immune response to oral pathogens and risk of preterm birth. *Am J Obstet Gynecol* . 2005;193(3):1121–6. doi:10.1016/j.ajog.2005.05.050.
25. Mikamo H, Kawazoe K, Sato Y. Intra-amniotic infection caused by capnocytophaga species. *Infect Dis Obstet Gynecol*. 1996;4:301–2.
26. Bearfield C, Davenport ES, Sivapathasundaram V, Allaker RP. Possible association between amniotic fluid micro-organism infection and microflora in the mouth. *BJOG: Int J Obstet Gynaecol*. 2002;109(5):527–33. doi:10.1111/j.1471-0528.2002.01349.x.
27. Michalowicz BS, Hodges JS, DiAngelis AJ, Lupo VR, Novak MJ, Ferguson JE, et al. Treatment of Periodontal Disease and the Risk of Preterm Birth. *N Engl J Med* . 2006;355(18):1885–94. doi:10.1056/nejmoa062249.
28. Newnham JP, Newnham IA, Ball CM, Wright M, Pennell CE, Swain J, et al. Treatment of Periodontal Disease During Pregnancy. *Obstet Gynecol* . 2009;114(6):1239–48. doi:10.1097/aog.0b013e3181c15b40.
29. Offenbacher S, Beck J. Effects of Periodontal Therapy on Rate of Preterm Delivery: A Randomized Controlled Trial. *Obstet Gynecol* . 2010;114(2):551–9.
30. Katz IA, Epstein S. Bone mineral metabolism at the menopause: determinants and markers. In: Humoral factors in the regulation of tissue growth. vol. 5. New York: Springer-Verlag; 1993. p. 211–23.
31. Reinhardt RA, Payne JB, Maze CA, Patil KD, Gallagher SJ, Mattson JS, et al. Influence of Estrogen and Osteopenia/Osteoporosis on Clinical Periodontitis in Postmenopausal Women. *J Periodontol*. 1999;70(8):823–8. doi:10.1902/jop.1999.70.8.823.
32. Allen IE, Monroe M, Connelly J, Cintron R, Ross SD. Effect of postmenopausal hormone replacement therapy on dental outcomes: systematic review of the literature and pharmacoeconomic analysis. *Manag Care Interface*. 2000;13:93–9.
33. Jeffcoat MK. Osteoporosis: A Possible Modifying Factor in Oral Bone Loss. *Ann Periodontol*. 1998;3(1):312–21. doi:10.1902/annals.1998.3.1.312.
34. Kornman KS, Loesche WJ. The subgingival microbial flora during pregnancy. *J Periodontal Res*. 1980;15(2):111–22. doi:10.1111/j.1600-0765.1980.tb00265.x.
35. Mealey BL, Moritz A. Hormonal influences: effects of diabetesmellitus and endogenous female sex steroid hormones on the periodontium. *Periodontology*. 2000;32:59–81.
36. Jonsson R, Howland BE, Bowden GHW. Relationships between Periodontal Health, Salivary Steroids, and Bacteroides intermedius in Males, Pregnant and Non-pregnant Women. *J Dent Res*. 1988;67(8):1062–9. doi:10.1177/00220345880670080101.
37. Pack ARC, Thomson ME. Effects of topical and systemic folic acid supplementation on gingivitis in pregnancy. *J Clin Periodontol*. 1980;7(5):402–14. doi:10.1111/j.1600-051x.1980.tb02013.x.
38. Rubin JS, Bottaro DP, Chedid M. Keratinocyte growth factor. *Cell Biology Int*. 1995;19:399–411.

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