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ENDOCRINOLOGICAL CHANGES IN THE ORAL CAVITY DURING PREGNANCY: PATHOLOGICAL PHYSIOLOGY

Abstract

Some striking observations have now been made about the role of sex hormones in the development of pathologic changes in the gingiva. It has been known for a long time that sex hormones contribute to the vascular changes in gingiva during pregnancy. Evidence now suggests that sex hormones also are capable of altering the normal sub-gingival flora and the immune response in the oral cavity, resulting in intense (pregnancy granuloma) and frequent gingivitis in pregnant women. Other problems that seem to appear in the oral cavity during pregnancy are discussed later and are for the most part unrelated to hormonal changes. These unrelated pathologic findings include periodontitis and dental caries. The special treatment and prevention needs of dental patients during pregnancy are also discussed.

Keywords: *pregnancy, hormonal balance, pathophysiology, oral mucosa*

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Hamiləlik dövründə ağız boşluğunda endokrinoloji dəyişikliklər: patoloji fiziologiya

Xülasə

Diş ətində patofizioloji dəyişikliklərin inkişafında cinsi hormonların rolu ilə bağlı bəzi maraqlı müşahidələr aparılmışdır. Cinsi hormonların hamiləlik zamanı diş ətindəki damar dəyişikliklərinə töhfə verdiyi uzun müddətdir məlumdur. İndiki araşdırmalar göstərir ki, cinsi hormonlar normal diş əti florasını və ağız boşluğunda immun reaksiyanı dəyişdirə bilir, nəticədə hamilə qadınlarda intensiv (hamiləlik qranuloması) və tez-tez diş əti iltihabı olur. Hamiləlik dövründə ağız boşluğunda görünən digər problemlər daha sonra müzakirə olunur və əksər hallarda hormonal dəyişikliklərlə əlaqəli deyildir. Bu əlaqəli olmayan patoloji tapıntılara periodontit və diş kariyesi daxildir. Hamiləlik dövründə stomatoloji xəstəliklərin xüsusi müalicə və profilaktika ehtiyacları da müzakirə olunur.

Açar sözlər: *hamiləlik, hormonal balans, patofiziologiya, ağız boşluğunun selikli qişası*

Introduction

The changes brought about in the maternal organism by the state of pregnancy are important, because in many instances they mimic pathophysiologic responses to disease. If the constellation of changes occurring normally in pregnancy are misinterpreted as signs of disease processes, the gravid or puerperal woman may be subjected to diagnostic and therapeutic interventions that are not only unnecessary but may also be dangerous to mother and fetus.

Because so many system-specific changes occur in the course of pregnancy, it is difficult to develop a total physiologic overview. There are, however, a number of well-described adaptive physiologic states that produce changes in human systems similar to those seen in pregnancy. These adaptive states may be used as models or constructs to help integrate the diverse alterations in physiologic systems that occur during the course of normal gestation. Among the physiologic states that produce adaptive changes similar to those seen in pregnancy are the presence of a moderate-sized arteriovenous fistula, acclimation to increased environmental or internal heating, and adjustments to increasing levels of circulating progesterone.

Models of pregnancy as a physiologically adapted state

Model I: Pregnancy as an Arteriovenous Fistula

Patients on chronic renal dialysis who have peripheral shunts constructed for purposes of dialysis typically have flow rates in their shunts of approximately 600 ml/minute (Newman, Takei, Klokkeveld, 2015). Because uteroplacental flow rates at term (nearly 600 ml/minute) (Strowitzki, Germeyer, Popovici et al, 2006) are essentially the same as those in the artificially produced shunts, it is not surprising that there are similarities between the cardiovascular changes in the shunted patients and cardiovascular alterations in the pregnant woman, particularly as she approaches term.

In both of these circumstances there is evidence of increased peripheral circulation, decreased peripheral resistance, increased heart rate, increased cardiac output, and increased plasma volume. This particular model can be used to explain a number of other changes related not directly to the shunting mechanism but to secondary changes produced by increased peripheral circulation, such as increased renal plasma flow and the physiologic alterations associated with increased renal perfusion.

Model II: Pregnancy as a State of Heat Adaptation

Abrams and associates and others (Martin, Dominguez, Avila, 2002; Amir, Brown, Rager, Sanidad, Zeng, 2020) have shown that there is a considerable temperature gradient between the mother and fetus. Aortic temperature measurements made in the pregnant ewe indicate that the fetal core temperature exceeds that of the mother by 0.5°C, which is a significant amount. Thermodynamics and the physics of heat transfer suggest that because of this temperature difference, the flow of heat from the fetus to the mother is relatively constant. As a result, the maternal organism must adjust her thermoregulatory system to permit increased heat loss to the environment. Aside from physical considerations, the need for maternal thermoregulatory adjustments is suggested by the observation that homeothermic mammals function within a very narrow range of internal temperatures. Extremes in either direction produce significant alterations in the function of fundamental systems responsible for the maintenance of life.

Responses of the homeothermic mammal to internal and environmental heating produce similar physiologic alterations. These include increased respiratory rate, increased cardiac output, increased heart rate, expansion of plasma volume, increased peripheral circulation, and a number of other changes similar to those seen in normal human gestation.

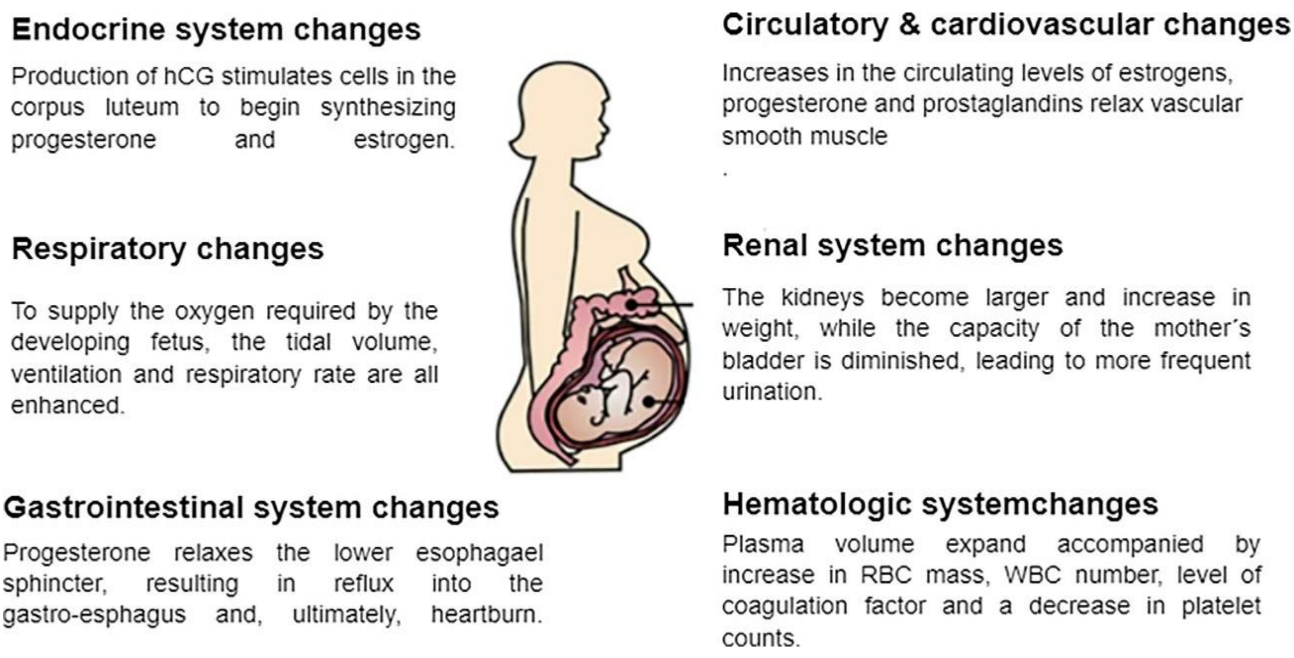
Model III: Pregnancy as a Hyperprogestational State

With the onset of normal gestation, all maternal systems are subjected to increasing levels of circulating progesterone. At first the corpus luteum of pregnancy, and later the placenta, produce large amounts of this hormone. At term, serum levels may be as high as 2.5 times those considered normal in the menstruating woman.

Increased basal body temperature and changes in the smooth muscle dynamics of the uterus, the vascular system, the urinary system, the gastrointestinal system, and the respiratory system in pregnancy have often been explained on the basis of increasing levels of serum progesterone. The mechanism proposed to explain many of these changes relates to the effect of progesterone on the electrochemical gradient at the cell membrane of individual smooth muscle fibers. According to this hypothesis, progesterone acts to hyperpolarize the cell membrane, depressing the resting electrical potential at the membrane to a level below that of the normal activation threshold. This effectively puts the muscle at rest, because much greater levels of stimulation are required to produce depolarization and subsequent muscle contraction. Decreased tone and overall decrease in contractile activity is seen in most of the structures that depend on smooth muscle for their action. This includes the uterus, gut, respiratory system, ureters, and peripheral vascular system.

Volume expansion of the intravascular space, decreased peripheral resistance, increased heart rate, and a number of other alterations associated with the pregnant state could theoretically be explained on the basis of progesterone's effect on smooth muscle.

Overall, it seems unlikely that a single model can be invoked to explain the varied changes that take place in the human female during the course of gestation. It is more likely that all of these mechanisms contribute, along with other factors still unidentified, to the myriad changes that constitute the physiologic alterations associated with the normal human gestation. Each model, nonetheless, helps the clinician to anticipate and integrate the changes in many of the altered systems. The constructs described permit the alterations in individual systems to be fused into a more coherent overview.



Changes in the Endocrine System

Already upon conception, the levels of certain hormones in a woman increase. Upon successful implantation of a fertilized egg into the uterine wall, placental trophoblasts begin to produce human chronic gonadotrophin (hCG) (Miller et al., 2020), the level of which rises during the first few weeks of pregnancy until it reaches its peak level of approximately 20000 mIU/mL during weeks 10-12, and thereafter, and at the end of the first trimester, falls steadily (Hendriks et al., 2019). hCG stimulates
cells in the corpus luteum to start producing progesterone and estrogen, the levels of which increase as pregnancy progresses and the placenta grows, reaching their peaks during the third trimester (Sykes and Bennett, 2018). In addition, the hCG hormone is involved in the formation of vessels and the placenta, the differentiation of fetal cells and growth of fetal organs and preventing premature contractions of the uterus musculature (Barjaktarovic et al., 2017).

The many processes mediated by progesterone include the adaptation of the cervix for implantation of the fetus and differentiation of stromal cells into decidual cells. Furthermore, increasing progesterone levels prevent uterine contractions both by diminishing the levels of receptors for prostaglandin and oxytocin and directly inhibiting the contraction of resident smooth muscle cells (Sykes and Bennett, 2018). Rising estrogen levels are responsible for neoangiogenesis and the formation of tissues that become the placenta and support lactation (Noyola-Martínez et al., 2019). These hormonal changes cause the typical fatigue, nausea, constipation, and headaches associated with early pregnancy (Fuhler, 2020). Moreover, the growing placenta also produces hormones, including human placental lactogen (HPL), relaxin and human chronic gonadotrophin.

The Oral Microbiome − The healthy human oral cavity contains approximately 50-100 million bacteria belonging to 700 species (Kilian et al., 2016), including Lactobacilli, Staphylococci, Streptococcus (Dewhirst et al., 2010; Kumar et al., 2013; Saadaoui et al., 2021). The composition of this complex community is affected by several factors, such as nutrition, oxygen levels, and pH (Saadaoui et al., 2021). Imbalances in the oral microbiome have been found to be associated with certain diseases, as well as with pregnancy. Imbalances in the oral microbiota, particularly during pregnancy, have been linked to a variety of disorders (Farrell et al., 2012). In fact, the oral microbiome of a healthy pregnant woman and a pregnant woman with certain diseases, e.g., gestational diabetes, differ.

The changes in microbiome that occur in connection with pregnancy include the microbiome in the oral cavity. For instance, the microbiome detected in saliva differs between pregnant and non-pregnant women, with the former showing an abundance of, e.g., Porphyromonas, Treponema and Neisseria, while in the latter, Veillonella and Streptococcus were overrepresented. The oral microbiome of pregnant women contain high numbers of bacteria, mainly during the first trimester including Porphyromonas, Neisseria, and Treponema and certain pathogenic bacteria. Moreover, certain specific species of bacteria, such as Staphylococci, Streptococci, Aggregatibacter actinomycetemcomitans, and Porphyromonas gingivalis, are more abundant in the oral microbiome during the first and second trimesters of pregnancy. During pregnancy, the proliferation and growth of Streptococcus, Lactobacillus, Escherichia coli, and Bifidobacterium species vary.

Furthermore, the hormonal changes that pregnant women undergo promote the formation of bacterial plaque, thereby resulting in gingivitis, especially during the second to third trimesters, which causes complications of pregnancy such as preeclampsia, preterm birth (PTB), low birth weight, and miscarriage. The amniotic fluid of a woman who went into preterm labor contained Fusobacterium nucleatum, suggesting that oral bacteria can translocate to the placenta. In another woman who suffered from gingivitis and gave an unusual full-term stillbirth, Fusobacterium nucleatum was detected in both the placenta and newborn infant, indicating that this bacterium originated from the maternal subgingival plaque. It appears possible that the environments in the oral cavity and placenta contain similar factors that promote colonization and growth of Fusobacterium nucleatum.

In addition, a positive correlation between the presence of a periodontopathogen (Porphyromonas gingivalis) and progesterone levels in the first trimester of pregnancy was observed. Other studies confirmed the growth of certain gram-negative anaerobic bacteria, including Prevotella nigrescens, Campylobacter rectus, and Prevotella intermedia, which is promoted by the hormonal changes that occur during pregnancy. Moreover, high estrogen levels promote infection by Candida.

Conclusion

The pregnant state is characterized by a myriad of alterations in the normal physiology of the gravid woman. An understanding of some of the major mechanisms that produce these changes is helpful in the analysis of symptoms and problems that arise during the course of a normal gestation. When associated disease is present, understanding of these alterations becomes more important in that they must be distinguished from pathophysiologic changes wrought by the disease process. The interaction between disease and gestational physiology may make the appropriate diagnosis and management of the pregnant woman difficult. When a pregnant woman requires medical or surgical therapy, the consultative services of an obstetrician or clinician trained in the complexities of maternal physiology is absolutely critical to the proper management of clinical problems.

References

1. Newman, M., Takei, H., Klokkeveld, P. (2015). Carranza’s Clinical Periodontology, 12th Edition, p.439, St. Louis. Saunders, Elsevier.
2. Strowitzki, T., Germeyer, A., Popovici, R. et al. (2006). The human endometrium as a fertility-determining factor. Human reproduction update.12:617-30.
3. Martin, J., Dominguez, F., Avila, S. et al. (2022). Human endometrial receptivity: gene regulation. Journal of reproductive immunology. 55:131-9.
4. Amir, M., Brown, J.A., Rager, S.L., Sanidad, K Z., Zeng, M.Y. (1999). Maternal Microbiome and Infections in Pregnancy. Microorganisms 8 (12). doi: 10.3390/microorganisms8121996
5. Staying-Healthy-During-Pregnancy: 4 Common Pregnancy Complications.
6. Miller, C., McQuade, M., MacCallum, J., Zhang, Y.V. (2020). Persistently Elevated hCG in a Patient With No Clear Evidence of Pregnancy. Clin. Chim. Acta 510, 703-706. doi: 10.1016/j.cca.2020.09.004
7. Hendriks, E., MacNaughton, H., MacKenzie, M.C. (2019). First Trimester Bleeding: Evaluation and Management. Am. Fam. Phys. 99 (3), 166-174.
8. Barjaktarovic, M., Korevaar, T.I., Jaddoe, V.W., de Rijke, Y.B., Visser, T.J., Peeters, R.P. et al. (2017). Human Chorionic Gonadotropin (hCG) Concentrations During the Late First Trimester Are Associated With Fetal Growth in a Fetal Sex-Specific Manner. Eur. J. Epidemiol. 32 (2), 135-144. doi: 10.1007/s10654-016-0201-3
9. Sykes, L., Bennett, P.R. (2018). Efficacy of Progesterone for Prevention of Preterm Birth. Best Pract. Res. Clin. Obstet. Gynaecol. 52, 126-136. doi: 10.1016/j.bpobgyn.2018.08.006
10. Noyola-Martínez, N., Halhali, A., Barrera, D. (2019). Steroid Hormones and Pregnancy. Gynecol. Endocrinol. 35 (5), 376-384. doi: 10.1080/09513590.2018.1564742
11. Fuhler, G.M. (2020). The Immune System and Microbiome in Pregnancy. Best Pract. Res. Clin. Gastroenterol. 44-45, 101671. doi: 10.1016/j.bpg.2020.101671
12. Kilian, M., Chapple, I., Hannig, M., Marsh, P., Meuric, V., Pedersen, A. et al. (2016). The Oral Microbiome-An Update for Oral Healthcare Professionals. Br. Dental J. 221 (10), 657-666. doi: 10.1038/sj.bdj.2016.865
13. Dewhirst, F.E., Chen, T., Izard, J., Paster, B.J., Tanner, A.C., Yu, W.H. et al. (2010). The Human Oral Microbiome. J. Bacteriol. 192 (19), 5002-5017. doi: 10.1128/JB.00542-10

14. Saadaoui, M., Singh, P., Al Khodor, S. (2021). Oral Microbiome and Pregnancy: A Bidirectional Relationship. J. Reprod. Immunol, p.103293. doi: 10.1016/j.jri.2021.103293
15. Farrell, J.J., Zhang, L., Zhou, H., Chia, D., Elashoff, D., Akin, D., et al. (2012). Variations of Oral Microbiota Are Associated With Pancreatic Diseases Including Pancreatic Cancer. Gut 61 (4), 582-588. doi: 10.1136/gutjnl-2011-300784

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