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A Review of Hormonal Changes During Pregnancy in Trimesters

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Abstract
The study of differences in physiology and function between the sexes is progressing. We are continuously learning more about the ways in which sex and the hormones generated during it impact not just cardiovascular problems, neuropathology, cancer therapy, circadian rhythms, and many other ailments. There are usually variations in physiological function between the different phases of the menstrual cycle because sex hormones impact so many physiological systems and organs. Research on endocrine diseases may be impacted by the significant physiological changes that take place in many organ systems, starting at conception and continuing during pregnancy. Practically every aspect of renal function is impacted by pregnancy. The coordination of the changes is a biological marvel.
The review paper focuses on how pregnancy-related hormonal changes impact kidney function and the physiological changes they cause. As part of the search methodology, extensive literature searches were carried out using electronic databases such as PubMed, Google Scholar, and Science Direct.

Keywords: Trimester, cardiovascular effects, hormonal changes, pregnancy, Endocrinology, Diabetes, Metabolism, Medical Education,

Overview

Research on endocrine diseases may be impacted by the significant physiological changes that take place in many organ systems, starting at conception and continuing during pregnancy. Thyroid hormone is controlled by a sensitive negative feedback loop. Thyrotropin-releasing hormone (TLRH) controls the release of thyroid hormones (thyroxine (T4) and triiodothyronine (T3) from the thyroid, which is controlled by the anterior pituitary. TSH is secreted by the pituitary. Numerous cell and organ processes, as well as metabolism, are impacted by thyroid hormone. The outward manifestations of thyroid disease are indicative of this crucial role. Disease progression is believed to be influenced by hormonal or genetic factors, and sex hormones, including progesterone, estrogen, prolactin, and androgens, are likely involved in the intricate mechanisms that underlie complicated diseases like multiple sclerosis (MS) [1]. Menopause and its course are significantly influenced by a number of hormone-related physiological events that affect women, including puberty, pregnancy, and childbirth.
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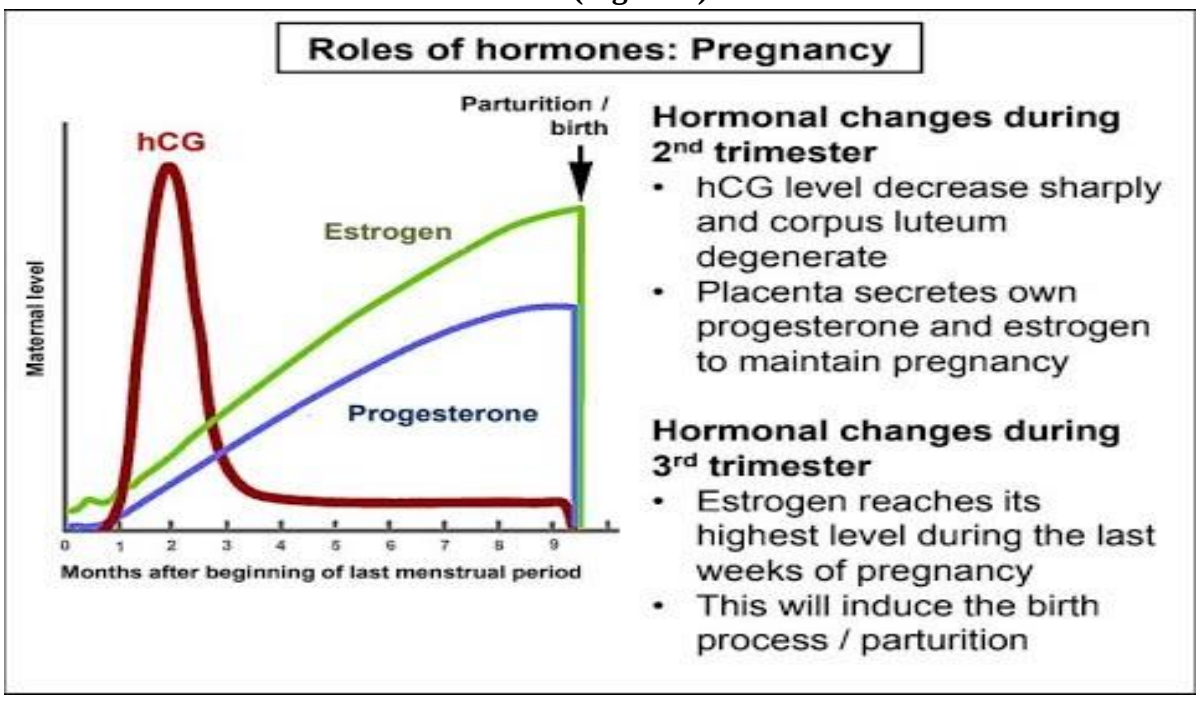
learning more about the ways in which sex and the hormones generated during it impact not just cardiovascular problems, neuropathology, cancer therapy, circadian rhythms, and many other ailments. There are usually variations in physiological function between the different phases of the menstrual cycle because sex hormones impact so many physiological systems and organs.

During pregnancy, almost all physiological systems experience considerable alterations. Even if the exact etiology of acne is unknown, a number of hormonal and physiological changes that take place throughout the various stages of pregnancy contribute to the development of the condition. The second and third trimesters are when pregnancy acne is most severe, often affecting the trunk and causing inflammation. Practically every aspect of renal function is impacted by pregnancy. The coordination of the changes is a biological marvel. Vasodilation and marked volume expansion indicate the state of the kidneys and the body's circulation. Comparing the renal plasma flow (RPF) and glomerular filtration rate (GFR) to pre-pregnancy values, increases of 80% and 50%, respectively, are observed.

Modest changes in tubular activity and water and electrolyte processing lead to a little increase in proteinuria and glucosuria, a decrease in serum osmolality, and a drop in blood salt levels. Fluid retention associated with pregnancy enlarges the kidneys and often leads to physiologic hydronephrosis [2].

An overview of the systems impacted and the hormones changed during pregnancy is provided below (Figure 1).

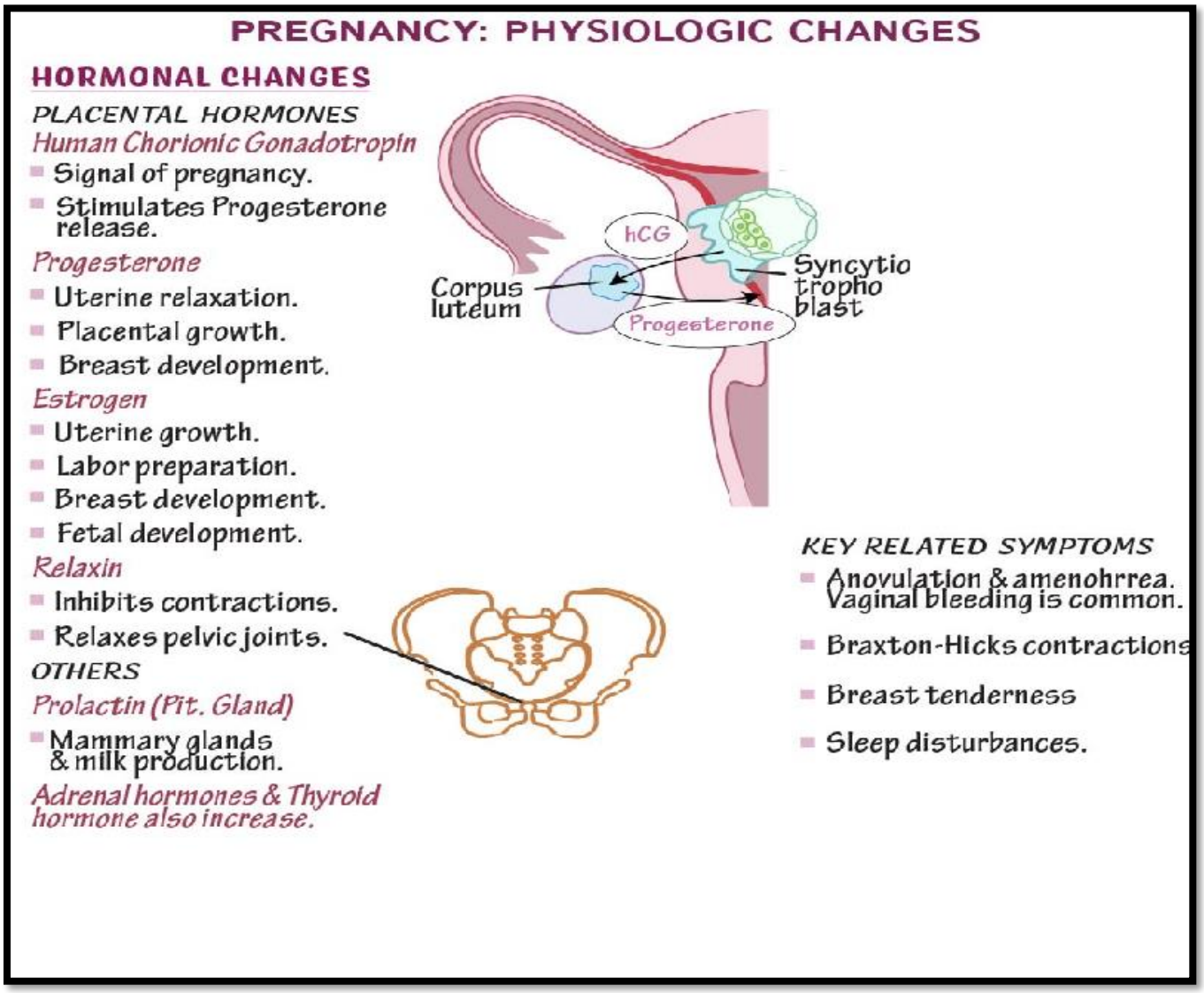


Methodology for searching

The review paper focuses on how pregnancy-related hormonal changes impact kidney function and the physiological changes they cause. As part of the search methodology, extensive literature searches were carried out using electronic databases such as PubMed, Google Scholar, and Science Direct. Search terms such as "renal function," "kidney," "physiological changes," and "pregnancy hormones" were used to locate relevant papers from the earliest to the latest publications. Studies with a range of demographics and experimental designs were taken into consideration, with an emphasis on the effects of pregnancy-related hormonal changes on renal physiology. The paper provides a comprehensive grasp of the intricate

relationships between hormonal changes and kidney function in pregnant women by synthesizing data from multiple papers.

Figure: 2 "Physiological Changes in Pregnant Women Due to Hormonal Changes"



The Thyroid

During pregnancy, the thyroid gland becomes more noticeable and experiences follicular hyperplasia. Human chorionic gonadotropin beta can activate TSH receptors. Due to increased liver synthesis and lower estrogen clearance, the level of thyroxine-binding globulin at the 20th week of pregnancy is two to three times more than it was before pregnancy. Consequently, women who take supplements in the early stages of pregnancy might need to take more thyroxine. As soon as it is feasible, pregnant patients with hypothyroidism should have their thyroid function examined. Due to immunoassay interference, a high biotin consumption may result in a picture resembling Graves' illness, with elevated fT4, high fT3, and heightened TSH receptor antibodies. The mother may produce thyroid hormone antibodies in reaction to fetal tissue epitopes, which could cause an aberrant increase in fT4 and fT3. Thyroid hormone is tested during amniocentesis.

The above information is depicted in tabular form in Table *1*.

Topic	Information
Thyroid changes during pregnancy	The thyroid gland enlarges and experiences follicular hyperplasia during pregnancy. The level of T3-binding globulin rises between two and three times by the 20th week due to increased liver production and decreased estrogen clearance.
TSH receptor activation	TSH receptors can be activated by beta-human chorionic gonadotropin.
Monitoring hypothyroidism in pregnant women	Pregnant women diagnosed with hypothyroidism should have their thyroid function checked as soon as practical.
Thyrotoxicosis causes during pregnancy	Graves' disease is a common cause of thyrotoxicosis during pregnancy.
Biotin interference and Graves' disease-like symptoms	Due to immunoassay interference, a high biotin intake can mimic Graves' illness with raised fT4, fT3, and heightened TSH receptor antibodies.
Thyroid hormone antibodies in pregnancy	Thyroid hormone antibodies may be produced by the mother in response to fetal tissue epitopes, potentially causing abnormal increases in fT4 and fT3.
Thyroid hormone measurement during amniocentesis	Thyroid hormone levels can be measured during amniocentesis, but caution is needed due to potential interference from antibodies created by the mother in response to fetal tissue epitopes.

TABLE 1: Thyroid level changes during pregnancy

Phosphorus and calcium-related level

There is a little drop in phosphate, calcium, and magnesium during pregnancy. Owing to an average decrease in albumin levels, the results of the adjusted calcium test could seem higher. Since ionized calcium levels don't change throughout pregnancy, measuring it is advised. In the second and third trimesters, there is an approximate 50% decrease in parathyroid hormone (PTH) levels and an increase in PTH-related peptide (PTHrP) concentrations. PTHrP, mostly placental, is the main hormone regulating calcium homeostasis and peaks during the third trimester of pregnancy. Due to increased calcium absorption and GFR, urine calcium excretion increases two to three times starting in the 12th week of pregnancy. Increased GFR and calcium absorption are the causes of this elevation in urine excretion; calcium excretion increases by two to three times. Research has demonstrated that urinary calcium concentrations in genetically identified familial hypocalciuric hypercalcemia cases during pregnancy increased to 8.6 mmol/L, urinary calcium/creatinine ratio of clearance was 0.02 and calcium concentration increased to 8.6 mmol/L with an increase in calcium correction to 3.35 mmol/L [3].

Furthermore, a decrease in serum magnesium throughout the third trimester resulted in a 30% drop in serum magnesium levels relative to pre-conception values. Ionized, RBC, and intracellular free magnesium concentrations in the brain and muscle are lower in pregnant individuals than in non-pregnant controls, according to observations made with nuclear magnetic resonance spectroscopy. Pregnancy causes the urine to discharge about 25% more magnesium.

Respiratory changes

The modifications in the central respiratory center's hormone and biochemistry, the growing fetus's mechanical modifications, or regional variations in the respiratory smooth muscle can all affect the respiratory physiology of mothers. Progesterone in the blood stimulates the respiratory center, leading to an increase in minute ventilation mostly in the form of a 40% increase in tidal volume and a 15% increase in respiratory rate. The respiratory system experiences a number of physiological and anatomical changes, such as increases in tidal volume, ventilation, and respiratory rate, to meet the growing fetus's increased oxygen requirements. During pregnancy, there is a decrease in expiratory reserve volume, total lung capacity, and functional residual capacity. This is mostly because the ligaments' elasticity has been impacted by elevated progesterone levels.

Renin, angiotensin, and aldosterone pathway

Plasma aldosterone concentrations increase three to eight times during pregnancy compared to non-pregnant levels, reaching a plateau in the third trimester. In a similar vein, the 24-hour urine aldosterone excretion during term pregnancy is around eight times higher than that during non-pregnancy. Plasma renin activity has increased four times by eight weeks of gestation and seven times at term. Decreases in aldosterone-to-renin ratios may have an impact on the main aldosteronism diagnosis. Dynamic testing for primary aldosteronism are typically avoided during pregnancy due to concerns about salt and volume in the loading process [4]. Results, however, are given after a saline infusion for expectant mothers in good health.

Prorenin levels in the blood did not rise in pregnancies without a corpus luteum. Prorenin increased during these pregnancies in a manner similar to the rise in renin in modesty, and prorenin and renin declined at the same time after delivery. Prorenin levels and corpus luteum number were further corroborated by recent data from 277 women who had no corpus luteum, one corpus luteum, or more than one corpus luteum. All of these results demonstrate that while the kidneys promote renin upregulation throughout pregnancy, the ovaries are the primary source of prorenin levels in expectant mothers.

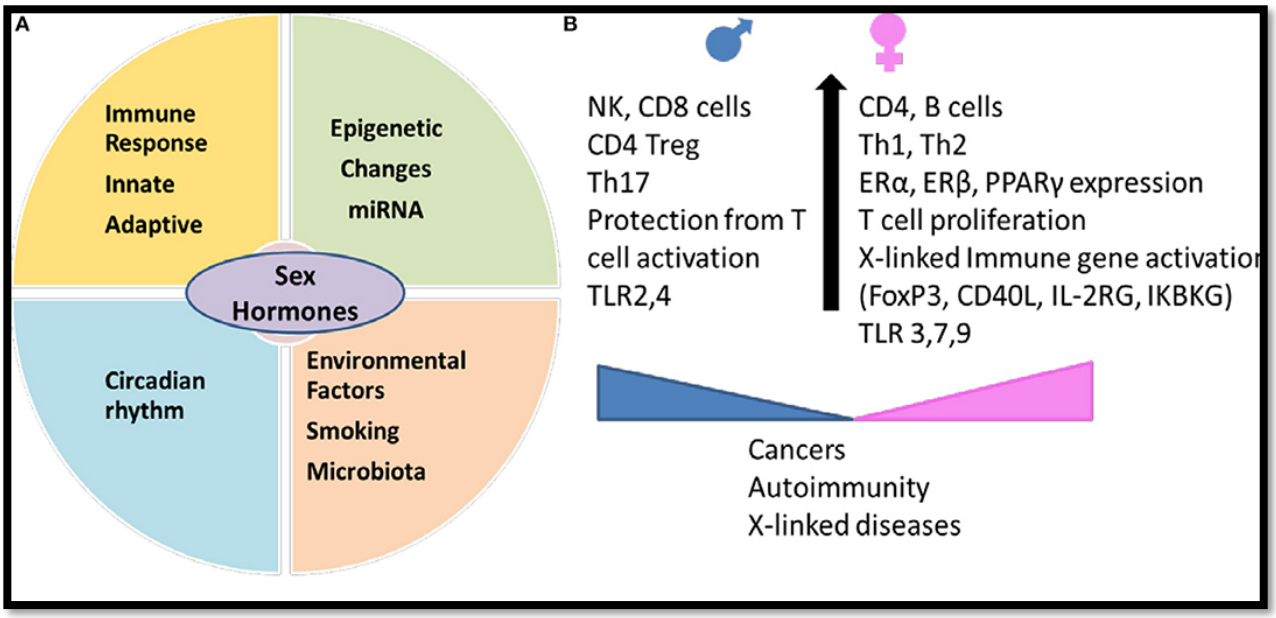
Cardiovasular changes

The majority of cardiovascular alterations occur in the early stages of pregnancy. Vascular smooth muscle relaxes in response to elevated progesterone, estrogen, and prostaglandin levels in the blood, reducing systemic and pulmonary vascular resistance. During the third trimester, cardiac output gradually increases and might eventually rise by 30 to 50 percent. Ventricular hypertrophy, which also raises heart rate and stroke volume, is the reason of the rise in cardiac output. Pre-eclampsia (PET) is a pregnancy-related illness marked by hypertension, or elevated blood pressure, and organ damage, usually to the kidneys and liver. If PET is not treated, it often manifests after 20 weeks of gestation and may result in difficulties for the mother and the unborn child. Although cardiac troponin I levels are unaffected in healthy pregnancies in as many as 25% of PET-complicated conceptions, it is crucial to investigate the risk of myocardial injury when a woman has substantial pulmonary edema and PET abnormalities in diabetic pregnancies. Three to six months after labor, elevated levels of brain natriuretic peptide may not disappear in relation to chronic hypertension, gestational hypertension, and PET. Coronary angiography can be performed risk-free during pregnancy[5].

Sexual hormone

Increased blood levels of reproductive hormones, including progesterone and estrogen, are linked to numerous physiological alterations associated with pregnancy. Furthermore, the placenta secretes hormones such as relaxin, human placental lactogen, and human chorionic gonadotropin that affect multiple body systems. Throughout pregnancy, estradiol levels gradually increase; by the third trimester, they have multiplied 100 times from prenatal levels. Progesterone and 17-hydroxyprogesterone levels are likewise obviously and consistently rising. Increases in prenatal testosterone levels are noted and multiplied by five. The sex hormone-binding globulin levels rise by approximately five times during pregnancy. Elevated estrogen levels initiate neo-angiogenesis, the development of tissues that support lactation and eventually become the placenta. The typical pregnancy symptoms of weakness, vomiting, bowel motions, and headache are brought on by these endocrine changes.

Sex hormones such as estrogen, progesterone, androgens, and prolactin can influence multiple aspects of immune system function and potentially impact MS development, activity, and risk because immune cells have hormone receptors[6]. The effects of sex hormones will vary depending on the kind of target cell, the receptor subtype expressed on that cell type, and the hormone concentration.



The Impact of sex hormones on immune cells is described in Table 2.

Renal changes

Renal blood flow and GFR increased by 50% in tandem with the increase in cardiac output. Serum urea and creatinine from pre-pregnancy values may drop by 40%. As glomerular filtration surpasses renal absorption of these molecules (along with other molecules like bicarbonate and other electrolytes) urine protein and glucose levels rise. Progesterone can raise GFR and RPF, but it is unable to account for the magnitude of the rise observed during pregnancy. The vasodilator hormone relaxin is released by the corpus luteum, decidua, and placenta. Increased vascular gelatinase activity working via the endothelium endothelin B receptor-nitric oxide pathway is linked to renal physiology in pregnant animals. One of the most typical signs of pregnancy is frequent urination, which is brought on by the developing fetus's

immense pressure on the mother's bladder. Furthermore, a 50% increase in GFR and a 50% drop in serum creatinine levels can result from increased renal blood flow [7].

Hematological changes

During the first trimester, there is an increase in WBC counts, particularly in neutrophils, due to the physiological load that comes with pregnancy. This is most likely because pregnant neutrophils are less able to undergo apoptosis, which is most likely caused by an increase in inhibitory substances in the serum. Throughout pregnancy, the number of myelocytes and metamyelocytes also increases, indicating stronger marrow activity and increased erythrocytes[8]. Furthermore, in the first and second trimesters, the lymphocyte count drops, and in the third trimester, it increases. Furthermore, research has demonstrated that platelet counts drop during pregnancy, especially in the third trimester. Gestational thrombocytopenia is a disorder caused by increased platelet activation and clearance in addition to hemodilution that happens during pregnancy.

During the peripartum phase, the hematological system experiences extensive modifications, and the risk of anemia, thromboembolism, and consumptive coagulopathies increases dramatically. Elevated secretion of aldosterone (due to renin-angiotensin axis activation) raises the body's total water content and plasma volume. Additionally, erythropoiesis rises by about 30% [9].

Gastrointestinal changes

During pregnancy, heartburn is common. This is explained by a decrease in the lower esophageal sphincter's tone, an increase in the amount of secretions, and a drop in the pH of gastric secretions. Lower esophageal sphincter tone is decreased as a result of progesterone activity on smooth muscle cells, which aggravates heartburn sensations and increases nausea and vomiting. Although the severity and presentation of nausea and vomiting can vary, it affects about 80% of pregnant people. It can begin as early as the second week of pregnancy, last through the second trimester, and, in certain cases, last until 37 weeks or full term [10].

Certain research have revealed slowed stomach emptying, especially early in pregnancy, in contrast to studies showing no delay in motility throughout pregnancy. Pregnancy-related delayed stomach emptying may affect how well some medications, including acetaminophen, are absorbed. Furthermore, concurrent use of many medications may result in altered absorption profiles in both pregnant and non-pregnant patients [11]. For example, patients are cautioned against taking iron supplements and proton pump inhibitors together since they may decrease the absorption of levothyroxine.

Conclusions

In summary, pregnancy is a significant physiological shift that is regulated by a complicated interplay of hormone fluctuations and entails minor adjustments to a variety of organ systems. To assess endocrine disorders at this critical period, it is imperative to understand these changes.
The endocrine system undergoes significant alterations, especially in the thyroid and its feedback pathways. A thorough consideration of variables such as biotin and possible interference from larger thyroid glands and increased thyroxine-binding globulin is necessary for an informed assessment. Calcium and phosphorus levels are also significantly impacted by pregnancy, which affects PTH and complicates the diagnosis of related illnesses.

Profound alterations in the renin-angiotensin-aldosterone pathway impact fluid equilibrium and could potentially modify diagnostic standards. Crucially, sex hormones influence immunological responses, which influence the development and progression of disease, especially in conditions like multiple sclerosis. The kidneys in the renal domain show altered electrolyte management and higher filtration rates to satisfy the demands of pregnancy. In order to meet these increased demands and lower risks, the hematological system is likewise constantly changing. These physiological changes—which are necessary for a successful pregnancy—highlight the need for pregnant patients to get carefully tailored medical care. A full comprehension of these intricate changes is essential for the best possible health of mother and fetus, since it will direct safe diagnostic and therapeutic strategies during this transformative phase.

Additional Information

Disclosures

- **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work.
- **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.
- **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work
- **Conflicts of interest:** There are no conflicts of interest.

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