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**BIOMEDICAL ENGINEERING**

**PHS 212 (HUMAN PHYSIOLOGY)**

Elucidate the physiological adaptations of the female to pregnancy?

CHANGES IN THE GASTROINTESTINAL SYSTEM

Nausea and vomiting are the most frequent complaints involving the gastrointestinal system and usually happen in early pregnancy while heartburn happen primarily in late pregnancy. The gums become hyperemic and edematous during pregnancy and tend to bleed. The muscular wall of the esophagus is relaxed and this may cause reflux, which in turn can lead to esophagitis and heartburn. The stomach and the intestines have decreased motility presumably due to the effect of progesterone on smooth muscle contractility. This causes an increase in the time that it takes for the stomach to empty. Reduced gastric secretion has also been documented and it could account for the improvement of peptic ulcers sometimes observed in pregnancy. Decreased motility of the large intestine may lead to constipation.

The liver is affected significantly by pregnancy. Cholestasis jaundice is considered to be the result of estrogen effect on elimination of bilirubin by the liver. The effect of estrogens also, is to increase protein synthesis in the liver, which leads to increased production of fibrinogen and binding proteins. The liver enzymes are usually unaffected with the exception of alkaline phosphatase, which is increased at approximately two fold to four fold that is a result of a placental production. Pregnancy increases the size and decreases the motility of the gall bladder. The decreasing motility and increase in volume, combined with changes in the bile's composition, explain the correlation between the incidence of cholelithiasis and pregnancy.

 MUSCULAR SKELETAL AND NEUROLOGIC SYMPTOMS

A number of women may experience backache in the upper back, which is secondary to muscle tension from increasing breast size and discomfort. Most women, however, experience low back pain secondary to muscular fatigue and strain that is caused by the changes in body balance from the growing uterus. Several patients also may experience pressure on nerve roots that in turn may lead to muscular spasms and pelvic joined pains secondary to bone ligament relaxation from the sex hormones. The changes that happen on the ligaments and the cartilage of the pelvic bones secondary to the sex hormones may also lead some women to present with gait alterations. Finally, a number of women may experience paresthesia (numbness and tingling of fingers and toes). A number of theories are suggested for the explanation of these symptoms. The fingers and upper extremities are effected if lordosis posture is extreme; the head and neck are flexed, putting strain on the brachial nerves and causing tingling of hands and arms. Toes and lower extremities are affected if gravid uterus presses on femoral veins and nerves supplying lower extremities, thus interfering with circulation and causing paresthesia. Edema may cause pressure and tingling of hands or feet, especially in hands when rising in the morning. Sometimes excessive edema of the hands may lead to carpal tunnel syndrome. Finally, Vitamin B deficiency, hypoglycemia and hyperventilation have been suggested as causes of these symptoms.

SKIN CHANGES

A number of changes take place in the skin of pregnant women. Mechanical stretching of the skin over the abdomen and breasts can lead to striae. The increased levels of estrogen and progesterone have also been implicated. Usually striae remain permanently with some change in color. Prevention may be achieved with moisturizing creams, especially those containing lanolin and other oily substances. It should be realized, however, that striae may develop despite any preventative measures.

Vascular spider nevi and palmar erythema happen also during pregnancy. There is no clear explanation for these changes, but they most likely represent the result of vasodilatation that happens in the skin during pregnancy. Chloasma and other pigmented lesions can happen as a result of increased melanocyte stimulating hormone activity which in turn is a result of increased estrogen and progesterone levels. These lesions usually begin at about five to six months’ gestation. One way that these lesions may be prevented is by the use of screening agents and avoidance of direct sunlight. Skin pruritus affects a number of women and it may be related to increased retention of bile salts in the skin secondary to estrogen effects. Scratching of the skin can then lead to infected excoriations. Local measures with anti-pruritic creams and lotions usually are sufficient.

CARDIOVASCULAR CHANGES

Of all changes that happen in pregnancy, the single most important is the one involving the cardiovascular system. Adequate cardiovascular adaptation secures good placental development and thus appropriate fetal growth.

In brief, the cardiovascular changes involve a substantial change in the blood volume, cardiac output, heart rate, systemic arterial blood pressure, systemic vascular resistance, oxygen consumption and alterations in regional blood flow of various organ systems.

 Blood Volume

Significant increases in the blood volume start taking place in the first trimester and continue until the mid-third trimester, at approximately the 32nd to the 34th week. Beyond this point in gestation, the blood volume plateaus. This pattern was established with studies that kept the patients in the left lateral position to avoid vena cava compression. However, studies that kept the patient in the supine position had controversial results indicating a decline in the blood volume after 34 to 36 weeks. The average absolute increase in blood volume during pregnancy is about 1600 ml and in terms of percent change one should expect a 40 to 50 percent increase above pre-pregnancy levels. The increase in the blood volume is achieved by a combination of increases in the plasma volume and the RBC mass. The calculated plasma volume expansion is approximately 1300 ml and the volume of the RBC increases about 400 ml. This discordance in the change between the cellular elements of the blood and the liquid portion leads to the so called "physiologic anemia of pregnancy". The mechanisms leading to hypervolemia in pregnancy are still not entirely understood and seem to be multifactorial. Increased estrogen levels in pregnancy cause increased production of renin from the kidneys, the uterus and the liver and thus cause elevated renin plasma levels. The increase in renin, which stimulates aldosterone secretion, is associated with sodium retention and an increase in total body water. The roll of atrial natriuretic factor (ANF) in mediating changes in fluid balance during gestation is still not clearly understood. On the other hand, increased levels of human chorionic somatomammotropin and prolactin increase the amount of erythropoiesis and thus causes the necessary increase in the red blood cell mass.

The increase in blood volume with pregnancy appears to serve the essential physiologic needs of both the mother and fetus. It ensures adequate supplies required for normal fetal growth and oxygenation even under circumstances that affect the maternal cardiac output (inferior vena cava compression). This increased blood volume also helps normal pregnant women to withstand hemorrhage equal to the volume of blood added to the circulation during the course of the normal pregnancy without any signs of decompensation.

 Cardiac Output

 It has been well established since the beginning of this century that the cardiac output increases an average of 50 percent during pregnancy. It is generally accepted that cardiac output begins to rise during the first trimester, probably around the tenth week of pregnancy and continues to rise up until the 24th week of gestation. Once it reaches the peak it stays rather stable. That was the case in most if not all of the studies that evaluated women in a left-lateral tilt while studies that placed women in the supine position have shown a rather false reduction in cardiac output which was primarily mediated by inferior vena cava compression.

 Cardiac output is a product of stroke volume and pulse rate. The rise in cardiac output early in pregnancy is disproportionately greater than the increase in heart rate, and therefore is attributable to augmentation in stroke volume. As pregnancy advances, heart rate increases and becomes a more predominant factor in increasing cardiac output. At the late stages of pregnancy, the stroke volume declines to normal, non-pregnant values.

 The effect of maternal posture on cardiac output was demonstrated by a number of studies. A significant decrease (25 to 30 percent) in cardiac output, measured by dye dilution technique, was demonstrated in the supine position between the 38th and 40th weeks of pregnancy but not before the 24th week. These findings were confirmed recently by echocardiographic studies. Since heart rate was not affected significantly, positional decline in cardiac output was due to decreased stroke volume. The fall in cardiac output was also not associated with a significant change in blood pressure. This is probably due to an increase in peripheral vascular resistance.

 As many as 11 percent of women when placed in the supine position, will develop symptomatic hypotension and drop in the cardiac output which may lead to a loss of consciousness. These symptoms are relieved promptly with left-lateral positioning. In these particular patients who develop the symptoms, the cardiac output is not maintained despite the fact that they develop a significant increase in their heart rate. It is believed that the patients who become symptomatic are those who lack sufficient paravertebral collateral circulation to permit blood from the legs and the pelvic organs to bypass the occluded inferior vena cava.

 CHANGES IN THE REPRODUCTIVE SYSTEM

 Rhythmic tightening’s of the uterus occur as part of preparatory changes for labor. These are called Braxton-Hicks contractions and since the advent of ultrasound, can be seen as early as eight to nine weeks. As the pregnancy advances these contractions become more frequent and they are more likely to be felt by the patient. Usually they happen every 5 to 20 minutes and sometimes they may last as long as 30 minutes.

 The genital organs undergo significant changes with increased vascularity of the cervix and increased mucous formation by the cervical glands due to increased levels of estrogen. The vulva and the vagina are also edematous and present increased desquamation and transudation. This leads to an increase in the secretions from the vagina manifesting as increased leucorrhea. The secretions of the vagina are acidic because of the conversion of an increased amount of glycogen in the vaginal epithelial cells by Doderlein's Bacilli into lactic acid.

 Many patients experience perineal pressure pain, which may be secondary to vascular engorgement of tissues due to estrogen and stasis of blood and to pressure from fetal presenting parts. Pubic pain is also noted and may be secondary to increased joint motility that happens secondary to progesterone's relaxing effect on the pubic symphysis cartilage. Many women experience pain in the region of the round ligament, which is secondary to stretching as the uterus grows.

RENAL PHYSIOLOGICAL CHANGES

 The changes in renal function during pregnancy are profound and are surpassed only by those of the cardiovascular system. Major anatomic as well as functional changes are apparent as shown in the following paragraphs.

Anatomic Changes

 The kidney size increases only slightly during normal pregnancy. However, the more striking in structural changes are those of the ureters, calyces, and renal pelvis. These changes are readily seen as early as the third month of gestation and remain until approximately the fourth month postpartum. Since these changes appear long before the gravid uterus is large enough to cause mechanical compression of the ureters, a hormonal effect is postulated. Progesterone, a smooth muscle relaxant, is produced in large concentrations even early in pregnancy, and is most likely the cause of the dilatation and decrease in peristaltic activity. Later in pregnancy, mechanical compression must certainly play a role. Interestingly, the dilatation of the upper urinary tract is greater on the right than on the left. The explanation given by some for this phenomenon is that the colon acts as a cushion to protect the left ureter, whereas the right ureter is more exposed.

Functional Changes

 Of all functional renal changes that accompany pregnancy, the most striking is that of glomerular filtration rate (GFR), which increases by approximately 50 percent. Renal plasma flow on the other hand increases by approximately 25 percent. Both begin to change early in the second trimester of pregnancy and in lateral recumbence are maintained at these elevated levels to term. The factors responsible for these changes remain conjectural, but the following have been suggested; 1) The growth hormone-like effect of the hormone human placental lactogenic, 2) The increased production and plasma concentration of free cortisol, 3) The increase in blood volume, 4) The hem dilution and hydremic resulting in decreased colloid osmotic pressure. Regardless of etiology, these functional alterations force us to redefine normal values of renal function during pregnancy. The normal serum creatinine in pregnancy drops to 0.46 mg.% as compared with the no pregnant value of 0.67 mg.%. The BUN decreases to 8.2 mg.% from a non-pregnant value of 13 mg.%. Uric acid also declines to a value of 3.1 mg.% from approximately 4.5 mg.%. The upper-normal uric acid level in pregnancy is 5 mg.% and levels higher than that should raise suspicion of preeclampsia. Creatinine clearance values increase to 150 - 200 ml/min as compared with values of 65 to 145 ml/min in the non-pregnant patient.

 Although a glomerular tubular balance exists for sodium during pregnancy, this is not the case for glucose or amino acids. The increased glomerular filtration rate leads to a significant glucose excretion that exceeds the tubular maximum for glucose reabsorption leading to glycosuria in many normal patients.

 A similar aminoaciduria is frequently seen in pregnancy. In compensation for the hyperventilation and hypocarbia that occur with pregnancy, there is an increase in bicarbonate excretion by the kidney. This results in an elevation of urine pH. During pregnancy there is a reversal of the usual non-pregnant diurnal pattern of urinary flow. When pregnant women go to bed at night third spaced fluid is mobilized and returns into the cardiovascular system leading to rather dilute urine in the morning, which is unusual according to non-pregnant standards. When tubular function tests are to be contacted in pregnant women, these effects should be taken in account and it may be best to collect urine from women for this test in the evening hours.

Posture and Renal Function in Pregnancy

 In non-pregnant individuals the up-right posture causes extra cellular fluid to shift to the legs, resulting in a relative decrease in central blood volume. This response is exaggerated during pregnancy and a similar response also occurs when the supine position is assumed. The extent of the change is a 50 to 60 percent decrease in urine flow and sodium excretion in supine recumbency versus lateral recumbency, accompanied by 20 percent decrease in renal plasma flow and glomerular filtration. The underlying patho-physiology is likely to be inferior vena cava obstruction, resulting in pulling of blood in the dilated veins of the lower extremities, dependent edema, decreased venous return, decreased central blood volume, increased aldosterone production, and ultimately decreased urinary excretion of sodium and water.

 In summary, one has to remember that the normal values of renal function are altered appreciably and that values normal to the non-pregnant could indicate substantial renal impairment in the pregnant patient.