PHYSIOLOGY ASSIGNMENT 3
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Question: Physiological adaptation of a female to pregnancy

Answer:

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PHYSIOLOGICAL ADAPTATIONS TO PREGNANCY

INTRODUCTION

Pregnancy is a unique period in a woman's lifetime. A number of anatomic, physiologic, biochemical and psychological changes take place. These changes may easily be misinterpreted by physicians who lack experience in regards to pregnancy effects on a woman's body. It is important that physicians caring for women understand the implications of these physiological changes in order to avoid any diagnostic errors and errors of management.

One has to remember that nature does not waste energy or effort. In that respect all the physiological changes that happen during pregnancy, happen for a purpose. As it will be appreciated later on in this chapter, almost every organ system of a female body is affected to some degree.

An attempt was made to present the information by organ systems although there may be some overlap since most of the organ systems interact with each other and affect each other. Some organ systems will be discussed in detail more than others. This distinction will be solely based on the significance of the particular organ system changes.

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.

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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.

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. Cholestatic

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

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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.

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.

Heart Rate During Normal Pregnancy

The baseline heart rate increases by about 10 to 20 beats per minute. This increase starts early in pregnancy and gradually

continues to go upward with the highest values achieved at term. Some investigators, however, suggested that the total increase happens early in pregnancy and remains so throughout the remainder of gestation.

In twin gestations, the rise of the heart rate is more pronounced and it can reach as much as 40 percent above the non-pregnant state. A change also from the supine position to the lateral position may cause the heart rate to drop slightly.

The Heart

A number of changes happen to the heart and are unique to pregnancy. Increasing intra-abdominal contents displace the heart upward with some forward rotation. As a result the anterior posterior diameter and the cardiothoracic ratio are increased. The overall dimensions of the heart are increased during pregnancy as a result of increased diastolic heart volume without any change in the ventricular wall

Systolic ejection murmurs are common in pregnancy while diastolic murmurs are less frequent. The systolic murmurs are usually the result of the hyperdynamic circulation.

Electrocardiogram changes have been reported during pregnancy. Transient ST and T changes are common in pregnancy, SRQ waves and inverted T waves in lead III. Left access deviation of the QRS complex has been reported also in pregnancy.

Blood Pressure

A slight decrease in the systolic arterial blood pressure and a significant decrease in the diastolic pressure have been observed to occur in normal pregnancy. This decrease becomes evident in the late first trimester and continues throughout most of the second trimester. The lowest values are noted in mid pregnancy and there after the blood pressure returns toward non-pregnant levels before term. The degree of change in the blood pressure parameters has been found to be affected by parity, smoking, preexisting hypertension, maternal age and ethnic background. In

the typical normal pregnancy the mean arterial pressure (diastolic plus 1/3 of the difference between systolic and diastolic) is less than 85 mm of mercury. Studies have found that when the mean arterial blood pressure in the mid second trimester is higher than 90 mm of mercury, there is increased perinatal mortality and morbidity.

Systemic Vascular Resistance

Normal pregnancy is associated with a significant fall in systemic vascular resistance. As a result, the diastolic blood pressure drops as well as the systolic. However, the diastolic blood pressure drops more than the systolic leading to a widening of the pulse pressure. The mechanism for this change is not entirely clear. It has been speculated, however, that a significant portion of this decline is caused by the development of a low resistance circulation in the pregnant uterus. Estrogens, Prolactin, circulating prostaglandins PGE_2 and PGI_2 may be responsible for the vasodilatation that can cause a drop in the peripheral resistance. In addition, the profound dilatation of the skin vessels as a result of the increased maternal body heat dissipation may contribute to the drop in the systemic vascular resistance.

Blood Flow Changes in Various Organ Systems During Pregnancy

The most profound changes in regional blood flow occur in the uterus with a 5 to 10 fold increase. This change starts early in pregnancy and continues until almost term. Approximately 20% of the maternal cardiac output perfuses the uterine vessels (placental and nonplacental). The kidneys also demonstrate substantial increase of the regional blood flow as much as 30 to 80 percent and at the same time a 50 percent increase in

glomerular filtration rate is noted. The regional blood flow in the extremities also increases and more so in the hands than the legs. As it was mentioned previously, there is a significant dilatation in the skin vessels which leads to an increase in the regional blood flow. These changes in the skin vessels may cause warm skin, clammy hands, vascular spiders, and palm erythema. The liver circulation is not affected very much and the same is true for the brain blood flow which is autoregulated. The blood flow to the breast is increased during pregnancy to prepare the breast for lactation. The effect of pregnancy on coronary blood flow is still unknown. It is safe, however, to speculate that an increase may happen since augmentation of cardiac function is present during pregnancy.

Cardiocirculatory Changes During Labor and Delivery

During labor significant hemodynamic changes take place. These changes can in part be explained by the effect of the uterine contractions, which may cause a significant increase of 300 to 500 ml in central blood volume, and in part by the effect of pain and anxiety on the cardiovascular system. It is important to note here that in the lateral position, cardiac output between contractions is higher than in the supine position and the increase during contractions is smaller.

The effect of uterine contractions during labor on the heart rate is variable. Some investigators have reported an increase in the heart rate and others have reported a decline in the heart rate. The differences may have to do with different position of the patient during the labor process and certainly different hemodynamic changes that can lead to the variability in the heart rate.

Significant variations of individual heart rate responses to uterine contractions may also play a role.

During labor (uterine contractions), both the systolic and diastolic blood pressures increase. The elevation of the blood pressure can be as high as 35 mm Hg in the systolic component and as high as 25 mm Hg in the diastolic component. As the labor process advances and the patient enters the second stage, an

increase in the diastolic blood pressure as high as 65 mm Hg above the baseline can be observed. It is believed that since the peripheral resistance does not change or it changes only slightly during labor, the increase in blood pressure is attributed to the rise in cardiac output. Redistribution of maternal cardiac output to the upper part of the peripheral circulation after compression of the distal aorta and the common iliac artery has also been suggested to play a role in the elevation of systemic pressures as measured in the arm. These hemodynamic changes are less pronounced in lateral recumbency than in the supine position.

The hemodynamic changes during labor are influenced to a great extent by the form of anesthesia or analgesia employed. The above-mentioned changes in the cardiac output and blood pressure did not happen on patients with caudal anesthesia. The progressive rise in the heart rate and the blood pressure that is normally observed is abolished on these patients and the stroke volume is also maintained throughout labor but rises rapidly after delivery.

In patients who undergo cesarean section maternal hemodynamics can be significantly affected by anesthesia. A patient with heart disease may not tolerate the marked fluctuations with subarachnoid block anesthesia. Balanced anesthesia with thiopental, nitrous oxide, and succinyl choline, and epidural anesthesia without epinephrine are associated with smaller hemodynamic fluctuations and therefore should be preferred in patients with limited cardiac reserves.

Hemodynamic changes in the postpartum period

In the postpartum period the blood volume decreases by about 10 percent on the patients who undergo vaginal delivery and 15 to 30 percent for those who undergo cesarean section. The cardiac output increases by 60 to 80 percent immediately after delivery and it rapidly decreases to a level slightly above the nonpregnant value. Complete return to normal nonpregnant values will take sometimes a few weeks. The stroke volume increases also significantly and the heart rate drops by 4 to 17 beats per minute shortly after delivery. Blood pressure is usually unchanged unless excessive blood loss has taken place in which case the blood pressure will drop or in other medical

complications. The peripheral vascular resistance according to some investigators is increased and according to others is unchanged.

PHYSIOLOGICAL RESPIRATORY CHANGES

Anatomic Changes

Mucosal edema and hyperemia secondary to capillary engorgement are common findings in the nasopharynx and the tracheal bronchial tract. In fact the majority of pregnant women have redness and swelling of the lungs that at times can produce changes in the voice. Changes also occur in chest circumference (6 to 7 cm.), vertical diameter (4 to 5 cm.), and the substernal angle (from 70 to 105 degrees). The increase in chest circumference compensates for the elevation of the diaphragm, so that essentially there is no change in the overall volume of the thoracic cavity.

Pulmonary Ventilation

During normal pregnancy the patients are in a state of hyperventilation. The arterial CO2 declines and the maternal arterial blood pH remains unchanged by compensatory increase in renal excretion of bicarbonate, which decreases to 21 mEq/L from 27 mEq/L. This hyperventilation of pregnancy seems to be related to the direct action of progesterone on the respiratory center. This effect with the lowering of the CO2 in the blood facilitates removal of CO2from fetal cells and produces CO2 in the fetus similar to what will be found in the newborn. During the labor process the hyperventilation process is augmented and the patients ventilation peak values can reach as high as 40 liters per minute as compared to the 12 liters per minute prior to labor. This is most likely attributable to the painful uterine contractions that lead to a spontaneous hyperventilation.

The oxygen consumption increases as pregnancy advances. The increase in oxygen consumption relates to the additional energy

requirements of the fetus as well as the other metabolic alterations that happen to the body of the pregnant woman. The total increment in basal oxygen consumption has been estimated at approximately 50 ml per minute. During labor, oxygen consumption rises during each uterine contraction from about 250 ml per minute to 750 ml per minute. The average oxygen consumption, which includes that during and between contractions, increases progressively and in the second stage approaches twice that of the term pregnant woman before the onset of labor.

During pregnancy the functional residual capacity of the lungs is decreased. The reduction has been attributed to the elevation of the diaphragm from the enlarging uterus. This effect is counterbalanced by a proportional increase in inspiratory capacity that results in an unchanged vital capacity. Overall

the respiratory changes in pregnancy reflect a tendency to assure plenty oxygen supply to the fetus and able opportunity to eliminate waste.

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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, where as the right ureter is more exposed.

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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 recumbency 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 lactogen, 2) The increased production and plasma concentration of free cortisol, 3) The increase in blood volume, 4)The hemodilution and hydremia 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 nonpregnant value of 0.67 mg.%. The BUN decreases to 8.2 mg.% from a nonpregnant 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 nonpregnant 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 glucosuria 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 caval 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.

CHANGES IN THE REPRODUCTIVE SYSTEM

Rhythmic tightenings 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 leukorrhea. 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.

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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 paresthesias (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 lordotic 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

paresthesias. 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.