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Question: Elucidate the physiological adaptations of the female to pregnancy

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. 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 pregnancy.

- 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.
- Adaptive changes in renal vasculature: The primary adaptive mechanism in pregnancy is a marked fall in systemic vascular resistance (SVR) occurring by week six of gestation. The 40% fall in SVR also affects the renal vasculature.4 Despite a major increase in plasma volume during pregnancy, the massive

decrease in SVR creates a state of arterial under-filling because 85% of the volume resides in the venous circulation.5 This arterial under-filling state is unique to pregnancy. The fall in SVR is combined with increased renal blood flow and this is in contrast to other states of arterial under-filling, such as cirrhosis, sepsis or arterio-venous fistulas.3,6

Relaxin, a peptide hormone produced by the corpus luteum, decidua and placenta, plays an important role in the regulation of haemodynamic and water metabolism during pregnancy. Serum concentrations of relaxin, already elevated in the luteal phase of the menstrual cycle, rise after conception to a peak at the end of the first trimester and fall to an intermediate value throughout the second and third trimester. Relaxin stimulates the formation of endothelin, which in turn mediates vasodilation of renal arteries via nitric oxide (NO) synthesis. Despite activation of the renin–angiotensin–aldosterone (RAA) system in early pregnancy, a simultaneous relative resistance to angiotensin II develops, counterbalancing the vasoconstrictive effect and allowing profound vasodilatation. This insensitivity to angiotensin II may be explained by the effects of progesterone and vascular endothelial growth factor mediated prostacyclin production, as well as modifications in the angiotensin I receptors during pregnancy. The vascular refractoriness to angiotensin II may also be shared by other vasoconstrictors such as adrenergic agonists and arginine vasopressin (AVP). It is possible that in the second half of pregnancy, the placental vasodilators are more important in the maintenance of the vasodilatatory state.

- **Body water metabolism:** Arterial under-filling in pregnancy leads to the

stimulation of arterial baroreceptors, activating the RAA and the sympathetic nervous systems. This results in a non-osmotic release of AVP from the hypothalamus. These changes lead to sodium and water retention in the kidneys and create a hypervolaemic, hypoosmolar state characteristic of pregnancy. Extracellular volume increases by 30–50% and plasma volume by 30–40%. Maternal blood volume increases by 45% to approximately 1 200 to 1 600 ml above non-pregnant values. By the late third trimester the plasma volume increases by more than 50–60%, with a lower increase in red blood cell mass, and therefore plasma osmolality falls by 10 mosmol/kg. The increase in plasma volume plays a critical role in maintaining circulating blood volume, blood pressure and uteroplacental perfusion during pregnancy. Activation of the RAA system leads to increased plasma levels of aldosterone and subsequent salt and water retention in the distal tubule and collecting duct. In addition to the increased renin production by the kidneys, ovaries and uteroplacental unit produce an inactive precursor protein of renin in early pregnancy. the placenta also produces oestrogen that stimulate the synthesis of angiotensinogen by the liver, resulting in proportionally increased levels of aldosterone compared to renin. Plasma levels of aldosterone correlate well with those of oestrogen and rise progressively during pregnancy. The increase in aldosterone is responsible for the increase in plasma volume during pregnancy. Progesterone, which is a potent aldosterone antagonist, allows natriuresis despite the sodium-retaining properties of aldosterone. The rise in GFR also increases distal sodium delivery, allowing excretion of excess sodium. Progesterone has antikaliuretic effects and

therefore excretion of potassium is kept constant throughout pregnancy due to changes in tubular reabsorption, and total body potassium increases during pregnancy.

Hypothalamic AVP release increases early in pregnancy as a result of increased relaxin levels. AVP mediates an increase in water reabsorption via aquaporin 2 channels in the collecting duct. The threshold for hypothalamic secretion of AVP and the threshold for thirst is reset to a lower plasma osmolality level, creating the hypo-osmolar state characteristic of pregnancy. These changes are mediated by human chorionic gonadotropin (HCG) and relaxin. In middle and late pregnancy there is a four-fold increase in vasopressinase, an aminopeptidase produced by the placenta. These changes enhance the metabolic clearance of vasopressin and regulate the levels of active AVP. In conditions of increased placental production of vasopressinase, such as pre-eclampsia or twin pregnancies, a transient diabetes insipidus may develop. As a consequence of this volume expansion, the secretion of atrial natriuretic peptides increases by 40% in the third trimester, and rises further during the first week postpartum. The levels of natriuretic peptides are higher in pregnant women with chronic hypertension and pre-eclampsia.