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PHARMACOLOGY

PHS 212- RENAL PHYSIOLOGY

ASSIGNMENT: ELUCIDIATE THE PHYSIOLOGICAL ADAPTATIONS OF THE FEMALE TO PREGNANCY

Hormonal : Pregnant women experience numerous adjustments in their [endocrine system](https://en.wikipedia.org/wiki/Endocrine_system) that help support the developing fetus. The fetal-placental unit secretes steroid hormones and proteins that alter the function of various maternal [endocrine glands](https://en.wikipedia.org/wiki/Endocrine_gland). Sometimes, the changes in certain hormone levels and their effects on their target organs can lead to [gestational diabetes](https://en.wikipedia.org/wiki/Gestational_diabetes) and [gestational hypertension](https://en.wikipedia.org/wiki/Gestational_hypertension).

**Fetal-placental unit:** Levels of progesterone and estrogen rise continually throughout pregnancy, suppressing the hypothalamic axis and subsequently the menstrual cycle. The progesterone is first produced by the [corpus luteum](https://en.wikipedia.org/wiki/Corpus_luteum) and then by the placenta in the second trimester. Women also experience increased [human chorionic gonadotropin](https://en.wikipedia.org/wiki/Human_chorionic_gonadotropin) (β-hCG), which is produced by the placenta.

**Pancreatic Insulin:** The placenta also produces [human placental lactogen](https://en.wikipedia.org/wiki/Human_placental_lactogen) (hPL), which stimulates maternal lipolysis and fatty acid metabolism. As a result, this conserves blood glucose for use by the fetus. It can also decrease maternal tissue sensitivity to insulin, resulting in [gestational diabetes](https://en.wikipedia.org/wiki/Gestational_diabetes)

**Pituitary gland:**The [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland) grows by about one-third as a result of hyperplasia of the lactrotrophs in response to the high plasma estrogen. [Prolactin](https://en.wikipedia.org/wiki/Prolactin), which is produced by the lactrotrophs increases progressively throughout pregnancy. Prolactin mediates a change in the structure of the breast [mammary glands](https://en.wikipedia.org/wiki/Mammary_gland) from ductal to lobular-alveolar and stimulates milk production.

**Parathyroid:** The fetal skeleton requires approximately 30 grams of calcium by the end of pregnancy. The mother's body adapts by increasing [parathyroid hormone](https://en.wikipedia.org/wiki/Parathyroid_hormone), leading to an increase in calcium uptake within the gut as well as increased calcium reabsorption by the kidneys. Maternal total serum calcium decreases due to maternal [hypoalbuminemia](https://en.wikipedia.org/wiki/Hypoalbuminemia), but the ionized calcium levels are maintained.

**Adrenal glands:** The increased estrogen in pregnancy leads to increase corticosteroid-binding globulin production and in response the [adrenal gland](https://en.wikipedia.org/wiki/Adrenal_gland) produces more cortisol. The net effect is an increase of free cortisol. This contributes to insulin resistance of pregnancy and possibly striate. Despite the increase in cortisol, the pregnant mom does not exhibit [Cushing syndrome](https://en.wikipedia.org/wiki/Cushing_syndrome) or symptoms of high cortisol. One theory is that high progesterone levels act as an antagonist to the cortisol.

The adrenal gland also produces more [aldosterone](https://en.wikipedia.org/wiki/Aldosterone), leading to an eight-fold increase in aldosterone. Women do not show signs of hyperaldosterone, such as hypokalemia, hypernatremia, or high blood pressure.

The adrenal gland also produces more [androgens](https://en.wikipedia.org/wiki/Androgens), such as testosterone, but this is buffered by estrogen's increase in sex-hormone binding globulin (SHBG). SHBG binds avidly to testosterone and to a lesser degree DHEA.

Breast size: A woman's breasts grow during pregnancy, usually 1 to 2 cup sizes] and potentially several cup sizes. A woman's torso also grows and her bra band size may increase one or two sizes. Once the baby is born up to about 50–73 hours after birth, the mother will experience her breasts filling with milk (sometimes referred to as “the milk coming in

Cardiovascular: The heart adapts to the increased cardiac demand that occurs during pregnancy in many ways.

* Cardiac output (Lit./Min.): 6.26
* Stoke Volume (Ml.): 75
* Heart Rate (Per min.): 85
* Blood Pressure: Unaffected

Cardiac output increases throughout early pregnancy, and peaks in the third trimester, usually to 30-50% above baseline. Estrogen mediates this rise in cardiac output by increasing the pre-load and stroke volume, mainly via a higher overall blood volume (which increases by 40–50%). The heart rate increases, but generally not above 100 beats/ minute. Total systematic vascular resistance decreases by 20% secondary to the vasodilatory effect of progesterone. Overall, the systolic and diastolic blood pressure drops 10–15 mm Hg in the first trimester and then returns to baseline in the second half of pregnancy. All of these cardiovascular adaptations can lead to common complaints, such as palpitations, decreased exercise tolerance, and dizziness.

Uterine Compression of IVC and Pelvic Veins. Displacement of PMI by Uterus

Uterine enlargement beyond 20 weeks' size can compress the inferior vena cava, which can markedly decrease the return of blood into the heart or preload. As a result, healthy pregnancy patients in a supine position or prolonged standing can experience symptoms of hypotension.

Hematology

**Blood volume and hemoglobin concentration:** Maternal Blood Volume

During pregnancy the [plasma](https://en.wikipedia.org/wiki/Blood_plasma) volume increases by 40-50% and the red blood cell volume increases only by 20–30%. These changes occur mostly in the second trimester and prior to 32 weeks gestation.

**Platelet and white cell count:** The effect of pregnancy on platelet count is unclear, with some studies demonstrating a mild decline in platelet count and other studies that show no effect. The white blood cell count increases with occasional appearance of myelocytes or metamyelocytes in the blood. During labor, there is a rise in leukocyte count.

**Hypercoagulability:** A pregnant woman will also become [hypercoagulable](https://en.wikipedia.org/wiki/Hypercoagulability" \o "Hypercoagulability), leading to increased risk for developing blood clots and embolisms, such as [deep vein thrombosis](https://en.wikipedia.org/wiki/Deep_vein_thrombosis) and [pulmonary embolism](https://en.wikipedia.org/wiki/Pulmonary_embolism). Women are 4-5 times more likely to develop a clot during pregnancy and in the postpartum period than when they are not pregnant. Hypercoagulability in pregnancy likely evolved to protect women from hemorrhage at the time of miscarriage or childbirth.

The increased risk of clots can be attributed to several things. Plasma levels of pro-coagulantion factors increased markedly in pregnancy, including: [von Willebrand Factor](https://en.wikipedia.org/wiki/Von_Willebrand_factor), [fibrinogen](https://en.wikipedia.org/wiki/Fibrinogen), [factor VII](https://en.wikipedia.org/wiki/Factor_VII), [factor VIII](https://en.wikipedia.org/wiki/Factor_VIII), and [factor X](https://en.wikipedia.org/wiki/Factor_X)

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| **Absolute and relative incidence of venous thromboembolism (VTE) during pregnancy and the postpartum period** |

**Edema:** [Edema](https://en.wikipedia.org/wiki/Edema), or swelling, of the feet is common during pregnancy, partly because the enlarging uterus compresses veins and lymphatic drainage from the legs.

Metabolic: During pregnancy, both [protein metabolism](https://en.wikipedia.org/wiki/Protein_metabolism) and [carbohydrate metabolism](https://en.wikipedia.org/wiki/Carbohydrate_metabolism) are affected. One [kilogram](https://en.wikipedia.org/wiki/Kilogram) of extra [protein](https://en.wikipedia.org/wiki/Protein) is deposited, with half going to the [fetus](https://en.wikipedia.org/wiki/Fetus) and [placenta](https://en.wikipedia.org/wiki/Placenta), and another half going to [uterine](https://en.wikipedia.org/wiki/Uterus) contractile proteins, [breast glandular](https://en.wikipedia.org/wiki/Breast_gland) tissue, plasma protein, and [haemoglobin](https://en.wikipedia.org/wiki/Haemoglobin" \o "Haemoglobin).

**Body weight:** Some degree of weight gain is expected during pregnancy. The enlarging uterus, growing fetus, [placenta](https://en.wikipedia.org/wiki/Placenta), [amniotic fluid](https://en.wikipedia.org/wiki/Liquor_amnii), normal increase in body fat, and increase in water retention all contribute weight gain during pregnancy. The amount of weight gain can vary from 5 pounds (2.3 kg) to over 100 pounds (45 kg).]

**Nutrition**:Nutritionally, pregnant women require a caloric increase of 350 kcal/day and an increase in protein to 70 or 75 g/day] There is also an increased [folate](https://en.wikipedia.org/wiki/Folate) requirement from 0.4 to 0.8 mg/day (important in preventing [neural tube defects](https://en.wikipedia.org/wiki/Neural_tube_defects)). On average, a weight gain of 20 to 30 lb (9.1 to 13.6 kg) is experienced.

All patients are advised to take [prenatal vitamins](https://en.wikipedia.org/wiki/Prenatal_vitamins) to compensate for the increased nutritional requirements. The use of Omega 3 fatty acids supports mental and visual development of infants. Choline supplementation of research mammals supports mental development that lasts throughout life.

Renal and lower reproductive tract

Genitourinary Changes in Pregnancy: Progesterone causes many changes to the genitourinary system. A pregnant woman may experience an increase in the size of the kidneys and ureter due to the increase blood volume and vasculature. Later in pregnancy, the woman might develop physiological hydronephrosis and hydroureter, which are normal. Progesterone causes vasodilatation and increased blood flow to the kidneys, and as a result [glomerular filtration rate](https://en.wikipedia.org/wiki/Glomerular_filtration_rate) (GFR) commonly increases by 50%, returning to normal around 20 weeks [postpartum](https://en.wikipedia.org/wiki/Postpartum). The increased GFR increases the excretion of protein, albumin, and glucose. The increased GFR leads to increased urinary output, which the woman may experience as increased urinary frequency. Progesterone also causes decreased motility of the ureters, which can lead to stasis of the urine and hence an increased risk of urinary tract infection

Pregnancy alters the [vaginal microbiota](https://en.wikipedia.org/wiki/List_of_microbiota_species_of_the_lower_reproductive_tract_of_women) with a reduction in species/genus diversity. Physiological hydronephrosis may appear from six weeks.

Gastrointestinal

Changes in the gastrointestinal (GI) system during pregnancy are caused by the enlarging uterus and hormonal changes of pregnancy. Anatomically, the intestine and stomach are pushed up from their original positions by the enlarging uterus. While there aren't any intrinsic changes in the sizes of the GI organs, the portal vein increases in size due to the hyperdynamic state of pregnancy.

The increased occurrence of gallstones during pregnancy is due to inhibition of gallbladder contraction (as result of increased smooth muscle relaxation mediated by progesterone) and reduced biliary transportation of bile (mediated by estrogen) which results in [cholestasis of pregnancy](https://en.wikipedia.org/wiki/Cholestasis_of_pregnancy)

Nausea and vomiting of pregnancy, commonly known as “[morning sickness](https://en.wikipedia.org/wiki/Morning_sickness)”, is one of the most common GI symptoms of pregnancy. It begins between the 4 and 8 weeks of pregnancy and usually subsides by 14 to 16 weeks. The exact cause of nausea is not fully understood but it correlates with the rise in the levels of [human chorionic gonadotropin](https://en.wikipedia.org/wiki/Human_chorionic_gonadotropin), [progesterone](https://en.wikipedia.org/wiki/Progesterone), and the resulting relaxation of smooth muscle of the stomach.

[Constipation](https://en.wikipedia.org/wiki/Constipation) is another GI symptom that is commonly encountered during pregnancy. It is associated with the narrowing of the colon as it gets pushed by the growing uterus found adjacent it leading to mechanical blockade. Reduced motility in the entire GI system as well as increased absorption of water during pregnancy are thought to be contributing factors.

Dietary cravings and dietary as well as olfactory avoidance of certain types of food are common in pregnancy. Although the exact mechanisms of these symptoms are not fully explained, it is thought that dietary cravings may arise from the thought that certain foods might help relieve nausea. Hemorrhoids and gingival disease are two common pregnancy associated physical findings involving the gastrointestinal system. Hemorrhoids arise as a result of constipation and venous congestion that are common in pregnancy

Immune tolerance: The [fetus](https://en.wikipedia.org/wiki/Fetus) inside a pregnant woman may be viewed as an unusually successful [allograft](https://en.wikipedia.org/wiki/Allograft), since it genetically differs from the woman. In the same way, many cases of [spontaneous abortion](https://en.wikipedia.org/wiki/Spontaneous_abortion) may be described in the same way as maternal [transplant rejection](https://en.wikipedia.org/wiki/Transplant_rejection)

Musculoskeletal

Neuromechanical adaptations to pregnancy refers to the change in gait, postural parameters, as well as [sensory feedback](https://en.wikipedia.org/wiki/Perception), due to the numerous anatomical, physiological, and hormonal changes women experience during [pregnancy](https://en.wikipedia.org/wiki/Pregnancy). Such changes increase their risk for [musculoskeletal](https://en.wikipedia.org/wiki/Human_musculoskeletal_system) disorders and fall injuries. Musculoskeletal disorders include lower-back pain, leg cramps, and [hip pain](https://en.wikipedia.org/wiki/Hip_pain).

**Lumbar lordosis**

To positionally compensate the additional load due to the pregnancy, pregnant mothers often extend their lower backs. As the fetal load increases, women tend to arch their lower backs, specifically in the lumbar region of their vertebral column to maintain postural stability and balance. The arching of the lumbar region is known as lumbar [lordosis](https://en.wikipedia.org/wiki/Lordosis), which recovers the center of mass into a stable position by reducing hip [torque](https://en.wikipedia.org/wiki/Torque). According to a study conducted by Whitcome, et al., lumbar lordosis can increase from an angle of 32 degrees at 0% [fetal](https://en.wikipedia.org/wiki/Fetus) mass (i.e. non-pregnant women or very early in pregnancy) to 50 degrees at 100% fetal mass (very late in pregnancy). Postpartum, the angle of the lordosis declines and can reach the angle prior to pregnancy. Unfortunately, while lumbar lordosis reduces hip torque, it also exacerbates spinal shearing load, which may be the cause for the common lower back pain experienced by pregnant women.

**Males vs. females**

Given the demands of fetal loading during pregnancy and the importance of producing [offspring](https://en.wikipedia.org/wiki/Offspring) to the [fitness](https://en.wikipedia.org/wiki/Fitness_(biology)) of [human beings](https://en.wikipedia.org/wiki/Human), one can imagine that [natural selection](https://en.wikipedia.org/wiki/Natural_selection) has had a role in selecting a unique [anatomy](https://en.wikipedia.org/wiki/Anatomy) for the [lumbar region](https://en.wikipedia.org/wiki/Lumbar_vertebrae) in females. It turns out that there are sex differences in the lumbar vertebral column of human males and females, which ultimately helps mitigate some of the discomfort due to the fetal load in females. There are 5 vertebrae in the lumbar region for both males and females. However, the 3 lower vertebrae of a female's lumbar region are dorsally wedged while for males, only the lower 2 of the lumbar region are dorsally wedged. When a female arches her lower back, such as during fetal loading, having an extra dorsally wedged vertebra lessens the shearing force. This lumbar [sexual dimorphism](https://en.wikipedia.org/wiki/Sexual_dimorphism) in humans suggests high natural selection pressures have been acting to improve maternal performance in posture and locomotion during pregnancy.

**Evolutionary implication**

If natural selection has acted on the lumbar region of [*Homo sapiens*](https://en.wikipedia.org/wiki/Humans) to create this sexual dimorphism, then this sort of trait should also be apparent in the genus [*Australopithecus*](https://en.wikipedia.org/wiki/Australopithecus), [hominins](https://en.wikipedia.org/wiki/Hominini) that have been known to be habitually [bipedal](https://en.wikipedia.org/wiki/Bipedalism) for at least 2 million years after the earliest bipedal hominins. Currently there are 2 nearly complete australopith lumbar segments; one has three dorsally wedged vertebrae in the lumbar region while the other has two. An explanation for these findings is that the first one is a female, while the latter is a male. This sort of evidence supports the notion that natural selection has played a dimorphic role in designing the anatomy of the vertebral lumbar region.

**Postural stability**:The weight added during the progression of pregnancy also affects the ability to maintain balance.

**Perception**: Pregnant women have a decreased [perception](https://en.wikipedia.org/wiki/Perception) of balance during quiet standing, which is confirmed by an increase in anterior-posterior (front to back) sway. This relationship heightens as pregnancy progresses and significantly decreases [postpartum](https://en.wikipedia.org/wiki/Postnatal). To compensate for the decrease in balance stability (both actual and perceived), stance width increases to maintain postural stability.

**Response to perturbations:** Under dynamic [postural stability](https://en.wikipedia.org/wiki/Standing), which can be defined as the response to anterior (front) and posterior (back) translation perturbations, the effects of pregnancy are different. ***Initial sway***, ***total sway***, and ***sway velocity*** are significantly less during the third trimester than during the second trimester and when compared to non-pregnant women

Additionally, the time it takes for pregnant women (any stage of pregnancy) to react to a translational disturbance is not significantly different than that of non-pregnant women. This alludes to some sort of stability mechanism that allow pregnant women to compensate for the changes they experience during pregnancy.

**Gait**

[Gait](https://en.wikipedia.org/wiki/Gait_(human)) in pregnant women often appear as a “waddle” – a forward gait that includes a [lateral component](https://en.wikipedia.org/wiki/Lateral_(anatomy)). However, research has shown that the forward gait alone remains unchanged during pregnancy. It has been found that gait parameters such as gait [kinematics](https://en.wikipedia.org/wiki/Kinematics), ([velocity](https://en.wikipedia.org/wiki/Velocity), stride length, and [cadence](https://en.wikipedia.org/wiki/Cadence_(gait))) remain unchanged during the third trimester of pregnancy and 1 year after delivery. These [kinetic](https://en.wikipedia.org/wiki/Kinetic_energy) gait parameters suggest an increased use of hip [abductor](https://en.wikipedia.org/wiki/Abduction_(kinesiology)), hip [extensor](https://en.wikipedia.org/wiki/Extension_(kinesiology)), and ankle plantar [flexor](https://en.wikipedia.org/wiki/Flexor) muscle groups. To compensate for these [gait deviations](https://en.wikipedia.org/wiki/Gait_deviations), pregnant women often make adaptations that can result in musculoskeletal injuries. While the idea of "waddling" cannot be dispensed, these results suggest that exercise and conditioning may help relieve these injuries.

Respiratory

As the uterus and fetus continue to enlarge over time, the diaphragm progressively becomes more upwardly displaced. This causes less space to be available for lung expansion in the chest cavity, and leads to a decrease in [expiratory reserve volume](https://en.wikipedia.org/wiki/Lung_volumes) and [residual volume](https://en.wikipedia.org/wiki/Lung_volumes). This culminates in a 20% decrease in [functional residual capacity](https://en.wikipedia.org/wiki/Functional_residual_capacity) (FRC) during the course of the pregnancy.

Oxygen consumption increases by 20% to 40% during pregnancy, as the oxygen demand of the growing fetus, placenta, and increased metabolic activity of the maternal organs all increase the pregnant person's overall oxygen requirements. This increase in oxygen consumption paired with the decrease in FRC can potentially mean that pregnant people with pre-existing and/or [comorbid](https://en.wikipedia.org/wiki/Comorbidity) asthma, pneumonia, or other respiratory issues may be more prone to disease exacerbation and respiratory decompensation during pregnancy.