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PHARMACOLOGY

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Phs204

Question :

1. Physiology of lactation
2. Physiology of pregnancy in a normal woman

PHYSIOLOGY OF LCTATION

Lactation, secretion and yielding of milk by females after giving birth. The milk is produced by the mammary glands, which are contained within the breasts.In most species, milk comes out of the mother's nipples; however, the platypus (a non-placental mammal) releases milk through ducts in its abdomen. In only one species of mammal, the dayak fruit bat, is milk production a normal male function.

In some other mammals, the male may produce milk as the result of a hormone imbalance. This phenomenon may also be observed in newborn infants as well (for instance, witch's milk).

Galactopoiesis is the maintenance of milk production. This stage requires prolactin and oxytocin.

Preparation for Lactation

By the fifth or sixth month of pregnancy, the breasts are ready to produce milk. During the latter part of pregnancy, the woman's breasts enter into the lactogenesis I stage. This is when the breasts make colostrum, a thick, sometimes yellowish fluid.

At this stage, high levels of progesterone inhibit most milk production. It is not a medical concern if a pregnant woman leaks any colostrum before her baby's birth, nor is it an indication of future milk production.

At birth, prolactin levels remain high, while the delivery of the placenta results in a sudden drop in progesterone, estrogen, and human placental lactogen levels. This abrupt withdrawal of progesterone in the presence of high prolactin levels stimulates the copious milk production of the lactogenesis II stage.

When the breast is stimulated, prolactin levels in the blood rise and peak in about 45 minutes, then return to the pre-breastfeeding state about three hours later. The release of prolactin triggers the cells in the alveoli to make milk.

Colostrum

Colostrum is the first milk a breastfed baby receives. It contains higher amounts of white blood cells and antibodies than mature milk, and is especially high in immunoglobulin A (IgA), which coats the lining of the baby's immature intestines, and helps to prevent pathogens from invading the baby's system. Secretory IgA also helps prevent food allergies. Over the first two weeks after the birth, colostrum production slowly gives way to mature breast milk.

This has less water soluble vitamins, fat and sugar than mature milk but contains more proteins (particularly immunoglobulins) and fat soluble vitamins.

Lactogenesis

The alveolar epithelial cells responsible for milk production are polarised, highly differentiated cells and their function is to accumulate, synthesise, package and export the components of milk:

Water	90%
Lactose	7%
Fat	2%
Protein	1%
Minerals	0.2% (Ca2+, Fe, Mg, K, Na, P, S)
Vitamins	A, B, B2, C, D, E, K
pH	7.0

Energy Value 27 MJ.l-1

Regulation of Milk Production

Regulation of quantity and content of milk is largely under hormonal control, primarily prolactin.

During pregnancy, a high progesterone : oestrogen ratio favours the development of alveoli, but not secretion. With the delivery of the placenta, the source of the large amount of circulating steroids (more so progesterone) is removed allowing the alveoli to respond to prolactin. Breast milk begins to form within 24 – 48 hours.

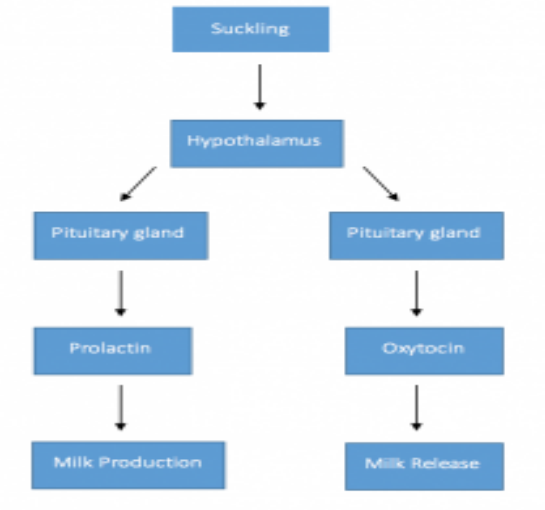
Prolactin is a polypeptide hormone and is secreted by the anterior pituitary gland. This is controlled by dopamine (also known as Prolactin Inhibiting Hormone) from the hypothalamus (inhibits prolactin). Factors promoting secretion of prolactin reduce dopamine secretion in a negative feedback loop. It is also produced by decidual cells.

Prolactin stimulation is promoted by suckling and is a neuro-endocrine reflex. Suckling mechanically stimulates receptors in the nipple and impulses pass up to the brain stem and to the hypothalamus to reduce the secretion of dopamine and increase vasoactive intestinal protein (promotes prolactin secretion). Suckling at one feed promotes prolactin release which causes production for the next feed which accumulates in alveoli and ducts (turgor).

Milk Let-Down Reflex

Mechanical stimulation of nipple is responsible for milk delivery to infant and maintenance of lactation. Babies do not suck the milk out of the breast, it is ejected by the let-down reflex. In response to suckling, oxytocin is released from the pituitary gland which stimulates myoepithelial cells that surround alveoli to contract thus squeezing milk out of the breast.

Despite suckling being the major stimulus for milk let down, the reflex can be conditioned. The cry or sight of an infant and preparation of the breast for nursing may cause let down, whereas pain, embarrassment or alcohol may inhibit it.



Maintaining Milk Production

The key to maintaining milk production is sufficient suckling stimulation at each feed to maintain prolactin secretion and to remove accumulated milk. If suckling stops, milk production ceases gradually. This is due to turgor induced damage to secretory cells and low prolactin levels. Milk suppression can also be achieved via steroids.

Prolactin secretion during lactation reduces fertility and so makes a new pregnancy less likely until the infant stops suckling.

PHYSIOLOGY OF PREGNANCY IN A NIRMAL WOMAN

Pregnancy is the time from fertilization of an egg, also known as conception, to birth. Getting pregnant and growing a human from scratch is a very complicated biological process that takes a lot of resources. As a result, pregnancy can have a wide range of effects on the mother, both physically and emotionally.

Each egg that is released during a menstrual cycle travels to your uterus. However, unlike unfertilized eggs that proceed unaltered and then disintegrate when they get there, a fertilized egg develops into a tiny human embryo on the way. On reaching the uterus, the embryo implants itself in the uterine wall, develops into a fetus, and steadily grows, until about nine months later it is ready to emerge into the outside world as a newborn baby.If you are fertile, sexually active, and become pregnant, the first thing you are likely to notice is a late or missing menstrual period. Fertilization of an egg triggers changes in the production of various hormones almost immediately, and hormone changes evolve and persist throughout your pregnancy to help you grow a healthy baby. Unfortunately, these changes may also cause unpleasant side effects. As a result, in addition to a

missed period, many women experience tender, swollen breasts, fatigue, nausea and vomiting, or morning sickness during the first few weeks of becoming pregnant.

Physiological changes that occur during pregnancy

Maternal physiological changes in pregnancy are the adaptations during pregnancy that a woman's body undergoes to accommodate the growing embryo or fetus. These physiologic changes are entirely normal, and include behavioral (brain), cardiovascular (heart and blood vessel), hematologic (blood), metabolic, renal (kidney), posture, and respiratory (breathing) changes. Increases in blood sugar, breathing, and cardiac output are all expected changes that allow a pregnant woman's body to facilitate the proper growth and development of the embryo or fetus during the pregnancy. The pregnant woman and the placenta also produce many other hormones that have a broad range of effects during the pregnancy

1.. Hormonal: The menstrual cycle refers to the normal changes in your ovaries and uterus that make an egg accessible for fertilization and prepare your uterus for pregnancy. It typically occurs once every 28 days. If you are ovulating normally, an egg, or ovum emerges from one or other of your ovaries, leaving behind a structure called the corpus luteum. This structure produces large amounts of progesterone and estrogen, hormones that help prepare your uterus for implantation of a fertilized egg. If the egg is not fertilized, the corpus luteum degenerates, causing progesterone and estrogen levels to drop, and menstruation to begin. If the ovum is fertilized, on the other hand, the corpus luteum remains intact and continues to maintain the hormone levels you need to keep your uterus baby-friendly. Eventually, the placenta develops the ability to secrete the necessary hormones itself, and the corpus luteum typically disappears after 3 to 4 months.In addition to progesterone and estrogen, human chorionic gonadotropin also spikes in early pregnancy. The levels of this hormone double every two days in the first 10 weeks of pregnancy. Its primary role is to prevent any further menstruation, and to prepare the placenta - the organ that connects the fetus to the uterus. The placenta allows the fetus to be supplied with nutrients and oxygen, as well as providing a route for the removal of toxic waste products. Although many signs and symptoms of pregnancy are related to hormonal changes, there are also many that occur due to the growing fetus invading the spaces that were previously occupied by your other organs.

2. Immune tolerance: The fetus inside a pregnant woman may be viewed as an unusually successful allograft, since it genetically differs from the woman. In the same way, many cases of spontaneous abortion may be described in the same way as maternal transplant rejectionYour growing fetus is a foreign object, something that your immune system is normally programmed to attack and reject. In order to prevent this from happening, as soon as the embryo becomes implanted in the uterine wall, a key pathway that usually triggers the launch of an immune attack is turned off, making this part of your immune system dormant, and preventing immune cells from targeting the fetus or placenta. In addition to making it possible for you to grow your baby, there can be secondary benefits of pregnancy-related changes in

immune function. In particular, women suffering from diseases caused by immune disorders, such as rheumatoid arthritis, multiple sclerosis, and psoriasis, may find relief from disease symptoms during pregnancy due to increased levels of anti-inflammatory steroids that occur naturally.

3. 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 pregnancyAll 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 UtUterus 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 hhypotension.

4 Hematologic: As cardiac output increases, blood volume increases to match. This is due to a 50% increase in the volume of your plasma (the clear, yellowish fluid of your blood), and a 20% increase in the number of red and white blood cells. Overall, this has the effect of diluting the blood, often resulting in “physiological anemia of pregnancy” (a relative deficiency of red blood cells). Iron requirements increase during pregnancy as the fetus and placenta grow, and as the red blood cell numbers rise. Iron is essential for red blood cell production, and supplements are often needed as the amount of iron absorbed from the diet and recruited from iron stores is often not enough. Several hormones are thought to play a role in changing blood composition to support pregnancy including the renin-angiotensin-aldosterone hormonal system, atrial natriuretic peptide, estrogen, and progesterone, although exactly how they do this is not clear. Whatever the mechanism, the increased blood volume is very important as it ensures that the extra blood needed to supply the growing uterus and placenta is available, and can help protect

the mother against normal blood loss that occurs while giving bbirth.

5. Metabolic: During pregnancy, both protein metabolism and carbohydrate metabolism are affected. One kilogram of extra protein is deposited, with half going to the fetus and placenta, and another half going to uterine contractile proteins, breast glandular tissue, plasma protein, and haemoglobin.An increased requirement for nutrients is given by fetal growth and fat deposition. Changes are caused by steroid hormones, lactogen, and cortisol.Maternal insulin resistance can lead to gestational diabetes. Increased liver metabolism is also seen, with increased gluconeogenesis to increase maternal glucose levels.

6. Renal: 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.[29] Progesterone causes vasodilatation and increased blood flow to the kidneys, and as a result glomerular filtration rate (GFR) commonly increases by 50%, returning to normal around 20 weeks postpartum.[17] 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.[5]Pregnancy alters the vaginal microbiota with a reduction in species/genus diversity.[30] Physiological hydronephrosis may appear from six weeks.

7. Respiratory: There are many physiologic changes that occur during pregnancy that influence respiratory status and function. Progesterone has noticeable effects on respiratory physiology, increasing minute volume (the amount of air breathed in and out of the lungs in 1 minute) by 40% in the first trimester via an increase in tidal volume alone, as the respiratory rate does not change during pregnancy.[39][40] As a result, carbon dioxide levels in the blood decrease and the pH of the blood becomes more alkaline (i.e. the pH is higher and more basic). This causes the maternal kidneys to excrete bicarbonate to compensate for this change in pH. The combined effect of the decreased serum concentrations of both carbon dioxide and bicarbonate leads to a slight overall increase in blood pH (to 7.44 compared to 7.40 in the non-pregnant state) . If an arterial blood gas (ABG) specimen is drawn on a pregnant person, it would therefore reveal respiratory alkalosis (from the decrease in serum carbon dioxide mediated by the lungs) with a compensatory metabolic acidosis (from the decrease in serum bicarbonate mediated by the kidneys).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 and residual volume. This culminates in a 20% decrease in 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 asthma, pneumonia, or other respiratory issues may be more prone to disease exacerbation and respiratory decompensation during pregnancy.

Your body undergoes massive changes to support and nourish a baby, and after giving birth, it generally takes some time for you to feel like yourself again. Some body changes that persist may take you by surprise, but are all linked to the physiological changes that were necessary to grow your baby. These are some of the most common ones:

- Low sex drive - this is linked to the abrupt drop in estrogen levels after you give birth. Your sex drive will come back, but don't be surprised if sex stays a low priority for you for the better part of a year.
- Tummy bulge - it takes 6-8 weeks for your uterus to shrink back to your pre-pregnancy size, meaning the tummy bulge may stick around for a while.
- Shoe size - you may notice that your feet swell during pregnancy, but for some women carrying the extra weight around permanently alters their shoe size. This is likely related to the effects of relaxin, which loosens the ligaments throughout your body including your feet. The extra weight during pregnancy can flatten your arches, making your feet grow.
- Breast size - although your breasts will grow during pregnancy and remain larger during breast feeding, it's not uncommon for them to shrink to a slightly smaller size than they were before you were pregnant. This is usually related to your body weight, as the size of your breasts depends on the amount of body fat you have.
- Hair loss - you may find your hair starts falling out faster than ever before during the months following childbirth. Estrogen slows the rate of hair loss during pregnancy, which means lots of hair is ready to drop when estrogen levels return to pre-pregnancy levels.
- Menstruation - if you decide not to breastfeed your baby, you are likely to start menstruating (and ovulating) again about 10 weeks after giving birth, as your hormones return to their pre-pregnancy levels. However, it's worth noting that your period may return the very next month after giving birth. Breastfeeding generally delays ovulation, so if you decide to breastfeed you may not have a period for up to 20 weeks or more, although it's also not uncommon for it to

restart earlier than this.