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«ГОМЕЛЬСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ»

Кафедра акушерства и гинекологии

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ФИЗИОЛОГИЯ БЕРЕМЕННОСТИ

Учебно-методическое пособие на английском языке
для студентов 4 и 6 курсов
факультета по подготовке специалистов для зарубежных стран
медицинских вузов

PHYSIOLOGY OF PREGNANCY

Teaching workbook in English
for 4 th and 6th year students
of the Faculty on preparation of experts for foreign countries
of medical highest educational institutions

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Предназначено для студентов 4 и 6 курсов факультета по подготовке специалистов для зарубежных стран медицинских вузов.

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PREFACE

Pregnancy is one of physiological conditions for women. For obstetricians and all doctors are conducted a survey is necessary to remember about physiological changes in female organism.

Likewise, non-obstetricians who see these women in consultation should be familiar with pregnancy-induced physiological changes that affect various diseases.

CHAPTER 1.
DIAGNOSIS OF PREGNANCY

The diagnosis of pregnancy usually begins when a woman presents with symptoms, and possibly a positive home urine pregnancy test result. Typically, such women receive confirmatory testing of urine or blood for human chorionic gonadotropin (hCG). There may be presumptive or diagnostic findings of pregnancy on examination. Sonography is often used, particularly in those cases in which there is a question about pregnancy viability or location.

Signs and Symptoms

Absence of Menses

The abrupt cessation of menstruation in a healthy reproductive-aged woman who previously has experienced spontaneous, cyclical, predictable menses are highly suggestive of pregnancy. Thus, amenorrhea is not a reliable indication of pregnancy until 10 days or more after expected menses onset. When a second menstrual period is missed, the probability of pregnancy is much greater.

Changes in Cervical Mucos

Dried cervical mucus examined microscopically has characteristic patterns dependent on the stage of the ovarian cycle and the presence or absence of pregnancy. Mucos crystallization necessary for the production of the fern pattern is dependent on an increased sodium chloride concentration. Cervical mucus is relatively rich in sodium chloride when estrogen, but not progesterone, is being produced.

In contrast, progesterone secretion — even without a reduction in estrogen secretion — acts promptly to lower sodium chloride concentration to levels that prohibit ferning. During pregnancy, progesterone usually exerts a similar effect, even though the amount of estrogen produced is enormous.

Breast Changes

Anatomical changes in the breasts that accompany pregnancy are characteristic during a first pregnancy. These are less obvious in multiparas.

In the early weeks of pregnancy, women often experience breast tenderness and paresthesias. After the second month, the breasts increase in size, and delicate veins become visible just beneath the skin. The nipples become considera-

bly larger, more deeply pigmented, and more erectile. After the first few months, a thick, yellowish fluid — *colostrums* — can often be expressed from the nipples by gentle massage. During the same months, the areolae become broader and more deeply pigmented. Scattered through the areolae are a number of small elevations, the *glands of Montgomery,* which are hypertrophic sebaceous glands. If the increase in breast size is extensive, striations similar to those observed in the abdomen may develop.

Abdominal Wall

After midpregnancy, reddish, slightly depressed streaks commonly develop in the abdominal skin and sometimes in the skin over the breasts and thighs. These are called *striae gravidarum* or *stretch marks.* In multiparous women, in addition to the reddish striae of the present pregnancy, glistening, silvery lines that represent the cicatrices of previous striae frequently are seen.

The muscles of the abdominal walls do not withstand the tension to which they are subjected. As a result, rectus muscles separate in the midline, creating a *diastasis recti* of varying extent.

Hyperpigmentation

The midline of the abdominal skin — *linea alba* — becomes especially pigmented, assuming a brownish-black color to form the *linea nigra.* Occasionally, irregular brownish patches of varying size appear on the face and neck, giving rise to *chloasma* or *melasma gravidarum* — the so-called *mask of pregnancy*. Pigmentation of the areolae and genital skin may also be accentuated. These pigmentary changes usually disappear, or at least regress considerably, after delivery. Oral contraceptives may cause similar pigmentation.

Melanocyte-stimulating hormone, a polypeptide similar to corticotropin, has been shown to be elevated remarkably from the end of the second month of pregnancy until term. Estrogen and progesterone also are reported to have melanocyte-stimulating effects.

Weight Gain

Most of the normal increase in weight during pregnancy is attributable to the uterus and its contents, the breasts, and increases in blood volume and extravascular extracellular fluid. A smaller fraction of the increased weight is the result of metabolic alterations that result in an increase in cellular water and deposition of new fat and protein — so-called *maternal reserves.*

Vaginal Mucosa

During pregnancy, the vaginal mucosa usually appears dark bluish- or purplish-red and congested — the *Chadwick sign,* popularized by him in 1886. Although presumptive evidence of pregnancy, it is not conclusive.

Cervical Changes

There is increased cervical softening as pregnancy advances. Other conditions, such as estrogen-progestin contraceptives, may also cause such softening.

As pregnancy progresses, the external cervical os and cervical canal may become sufficiently patulous to admit the fingertip. However, the internal os should remain closed.

Perception of Fetal Movements

Maternal perception of fetal movement may depend on factors such as parity and habitus. In general, after a first successful pregnancy, a woman may first perceive fetal movements between 16 and 18 weeks. A primigravida may not appreciate fetal movements until approximately 2 weeks later (18 to 20 weeks). At approximately 20 weeks, depending on maternal habitus, an examiner can begin to detect fetal movements.

Pregnancy Tests

Detection of Human Chorionic Gonadotropin (HCG) in maternal blood and urine provides the basis for endocrine tests of pregnancy. This hormone is a glycoprotein with a high carbohydrate content. The molecule is a heterodimer composed of two dissimilar subunits. HCG prevents involution of the corpus luteum, the principal site of progesterone formation during the first 6 weeks.

Trophoblast cells produce hCG in amounts that increase exponentially following implantation. With a sensitive test, the hormone can be detected in maternal plasma or urine by 8 to 9 days after ovulation.

After 7–9 days after fertilization the trophoblast begins to secrete human chorionic gonadotropin (hCG) — an indicator of the trophoblast's function. The corpus luteum in the ovary under the influence of hCG continues to develop and becomes the corpus luteum of pregnancy. The corpus luteum is a source of progesterone. The peak activity of the corpus luteum is achieved by 5–6 weeks, then its function to a 16–17 week quenched.

By 14–16 weeks completes the formation of the placenta. The placenta is a provisory organs of the fetus. The endocrine function of the placenta is a complex, self-regulated, it does not depend on the hypothalamic-pituitary influences. In placenta contains hCG, estrogen (estrone, estradiol, estriol), progesterone, corticosteroids, thyroid stimulating hormone, placental lactogen, androgens, vasopressin, a large number of biologically active substances such as histamine, acetylcholine, and etc.

Placental lactogen (PL) on the properties similar to growth hormone, has lactotrophic action, promotes the growth of mammary glands. PL is an antagonist of insulin, affects neither the carbohydrate, protein and fat metabolism.

Progesterone causes endometrial decidual transformation required for implantation of the blastocyst. Progesteron contributes to the development and growth of the uterus, its vascularization, reduces the excitability of the uterus, stimulates development of mammary glands, suppresses the immune response against the rejection of the fetus.

Estrogens The level of estradiol and estriol during pregnancy increases hundreds times compared to pre-pregnancy levels. Estrogens regulate biochemi-

cal processes in the uterus, increase the activity of enzymes, stimulates energy metabolism cause uterine vascularization, increase the sensitivity of the uterus to oxytocine substances.

Biologically active substances. Alpha-fetoprotein (a-FP) is produced in the yolk sac and fetal liver. In the early stages of pregnancy and its level increases from 10 weeks to 14 weeks maximum, then decreases. Its function is to protect the fetus from the mother's immune system, the binding of estrogen in the blood of the mother, participation in the fetal liver organogenesis.

Isolated from placental tissue specific protein nature substances pregnancy: trofoblastic 1-b-glycoprotein (TBG), pregnancy-associated protein A (PAPP–A), a2-macroglobulin (a2 M), placental proteins (PP–5, PP–10, PP–11, PP–12). The concentration of PAPP–A during pregnancy increases a thousand times.

CHAPTER 2.
PHYSIOLOGICAL CHANGES DURING PREGNANCY

During pregnancy we can see adaptive changes in healthy women.

Cardiovascular Changes

• *begin early in pregnancy;*

• *reach their peak during the second trimester, and then remain relatively constant until delivery;*

• *contribute to optimal growth and development of the fetus;*

• *help to protect the mother from the risks of delivery, such as hemorrhage.*

Hemodynamic changes in pregnant women include:

— Increase of blood volume.

— Disproportion between the volume of circulating plasma and red blood cells leads to physiological anemia.

— Reduction of blood viscosity.

— Increase of cardiac output.

— Increase of heart rate.

— Increase of venous pressure.

— Reduction of the total peripheral vascular resistance.

— Topographic and anatomical changes with the displacement of the heart’s axis.

Blood Volume

The well-known *hypervolemia* associated with normal pregnancy averages 40 to 45 percent above the nonpregnant blood volume after 32 to 34 weeks. For individual women, expansion varies considerably. For some there is only a modest increase, whereas in others the blood volume nearly doubles. A fetus is not essential for this because increased blood volume develops in case of hydatidiform mole.

Pregnancy-induced hypervolemia has important functions:

1.To meet the metabolic demands of the enlarged uterus with its greatly hypertrophied vascular system.

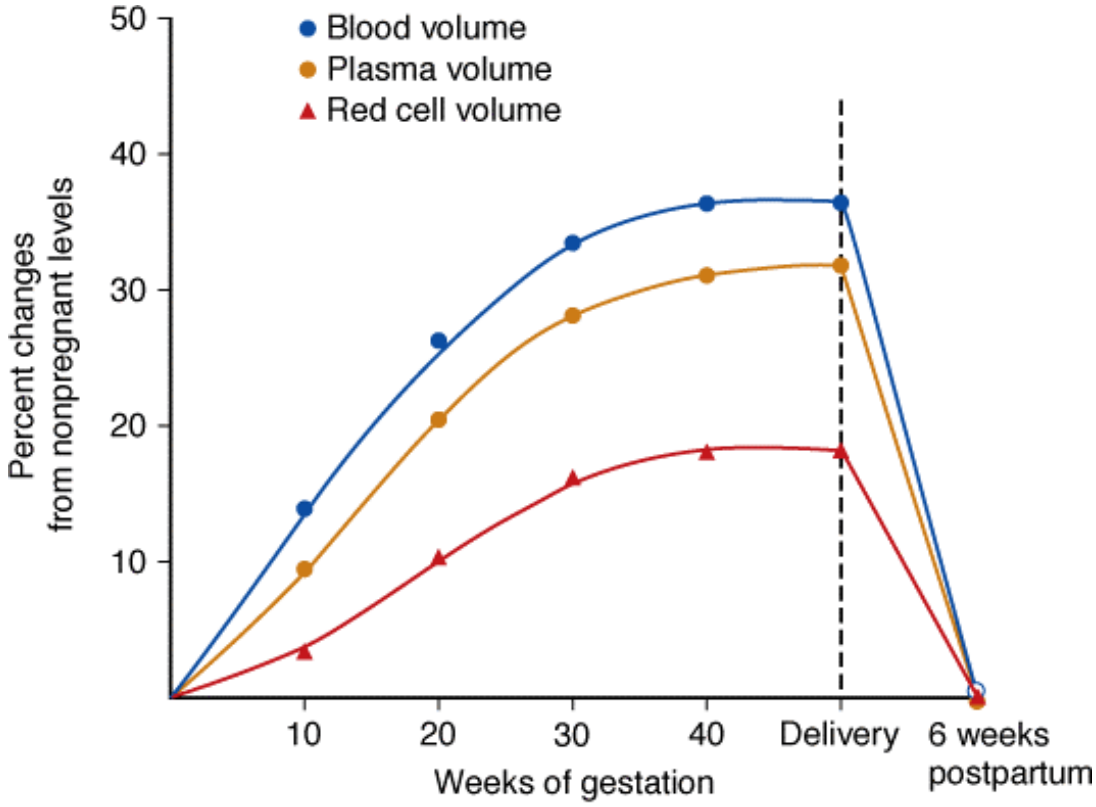
2.To provide an abundance of nutrients and elements to support the rapidly growing placenta and fetus.

3.To protect the mother and in turn the fetus, against the deleterious effects of impaired venous return in the supine and erect positions.

4.To safeguard the mother against the adverse effects of blood loss associated with parturition.

Maternal blood volume begins to increase during the first trimester and by 12 menstrual weeks, plasma volume expands by approximately 15 percent compared with that of prepregnancy. Maternal blood volume expands most rapidly during the second trimester — by 34 weeks up to 25–50 % of non-pregnant women. Then it rises at a much slower rate during the third trimester to plateau during the last several weeks of pregnancy.

The volume of red blood cells during pregnancy increases by 12–25 % (see picture 1). As a result of these changes, there is a physiological anemia of pregnancy. The hematocrit is 0,32–0,34/l, hemoglobin 105–110 g / l. These changes in the properties of blood in pregnant women are called *physiological hypervolemic autohemodilution.* Hematocrit value above 0.36 is a sign of hypovolemia or failure of autohemodilution's mechanisms and poor prognosis. During pregnancy varies not only red blood cells, but also their size and shape.



Picture 1 — Physiological hypervolemic autohemodilution

The increased volume of red blood cells increases their aggregation. High concentrations of hemoglobin in pregnant women in the 2nd and 3rd trimesters is a sign of the lack of increase in plasma volume, hemoconcentration, increased blood viscosity, reduced tissue perfusion. These processes are clinically characterized by some complications of pregnancy such as preeclampsia, chronic fetal hypoxia syndrome, intrauterine growth retardation and others.

Changes in cardiac function become apparent during the first 8 weeks of pregnancy. Cardiac output is increased as early as the fifth week and reflects a reduced systemic vascular resistance and an increased heart rate. Multiple factors contribute to these changes in overall hemodynamic function and allow the cardiovascular system to adjust to the physiological demands of the fetus while maintaining maternal cardiovascular integrity. Also we can observe the important effects of maternal posture on hemodynamic events during pregnancy.

During normal pregnancy, systolic and diastolic blood pressure decreased to the 2 trimester of 5–15 mm Hg, the maximum reduction occurs at 28 weeks, then returns to the pre-pregnancy digits. If blood pressure is higher than it was before during pregnancy, it is a sign of pregnancy complications or a reaction to stress (fear, anxiety, etc.).

Total peripheral vascular resistance is reduced by the formation of the mother circle of circulation, vasodilator action of estrogens and progesterone. During pregnancy normally appears tachycardia, by the end of pregnancy increases the heart rate by 15–20 beats per minute.

The growing uterus compresses the inferior vena cava. By the end of pregnancy the uterus weighs about 1 kg, the fetus together with the amniotic fluid around 5–6 kg. Under mechanical pressure to the inferior vena cava at women's supine position decreases the inflow of venous blood to the heart and reduced cardiac output, blood pressure falls. This condition may be associated with syncope, the so-called *syndrome of vena cava inferior*.

Late pregnancy is associated with the expected increases in heart rate, stroke volume, and cardiac output. Systemic vascular and pulmonary vascular resistance both decreased significantly, as did colloid osmotic pressure. Pulmonary capillary wedge pressure and central venous pressure did not change appreciably between late pregnancy and the puerperium.

Cardiac output is directly dependent on the amount of circulating plasma, heart rate, stroke volume, and increases to 26–32 week.

Due to the growing uterus, topographic changes increased intra-abdominal pressure, the diaphragm is lifted and shifting the axis of the heart. "Lying heart" is observed in 30 % of pregnant women. There is a functional systolic murmur at the apex, of the pulmonary artery, making it difficult to diagnose defects.

Progesterone level during pregnancy which increases relaxes vascular smooth muscle of the uterus and an increases in uterine vascular bed.

Hematological changes

In normal pregnancy with an increase in life there is a tendency to platelet aggregation, there is an increase in erythrocyte sedimentation rate, white blood cell count, neutrophil. These changes are not a sign of inflammatory reaction. The lower limit of normal hemoglobin should be considered as 110 g / l.

Because of great plasma augmentation, hemoglobin concentration and hematocrit decrease slightly during pregnancy. As a result, whole blood viscosity decreases. Thus, a hemoglobin concentration below 110 g/L, especially late in pregnancy, should be considered abnormal and usually due to iron deficiency rather than due to hypervolemia of pregnancy.

Of the approximate 1000 mg of iron required for normal pregnancy, about 300 mg are actively transferred to the fetus and placenta, and another 200 mg are lost through various normal routes of excretion, primarily the gastrointestinal tract. These are obligatory losses and occur even when the mother is iron deficient. The average increase in the total volume of circulating erythrocytes — about 450 mL — requires another 500 mg because 1 mL of erythrocytes contains 1.1 mg of iron. Because most iron is used during the latter half of pregnancy, the iron requirement becomes large after midpregnancy and averages 6 to 7 mg/day. This amount is usually not available from storage iron in most women, and the optimal increase in maternal erythrocyte volume will not develop without supplemental iron. Without supplementation, the hemoglobin concentration and hematocrit fall appreciably as the blood volume increases. At the same time, fetal red cell production is not impaired because the placenta transfers iron even when the mother has severe iron deficiency anemia. In severe cases, we have documented hemoglobin values of 3 g/dL and hematocrits of 10 percent.

It follows that the amount of dietary iron, together with that mobilized from stores, will be insufficient to meet the average demands imposed by pregnancy. If the nonanemic pregnant woman is not given supplemental iron, then serum iron and ferritin concentrations decline after midpregnancy. The early pregnancy increases in serum iron and ferritin are likely due to minimal iron demands early on combined with the positive iron balance from amenorrhea.

Leukocytes

Some polymorphonuclear leukocyte chemotaxis and adherence functions are depressed beginning in the second trimester and continuing throughout pregnancy. Although incompletely understood, this may be partly related to the finding that relaxin impairs neutrophil activation. It is possible that these depressed leukocyte functions of pregnant women also account in part for the improvement of some autoimmune disorders and possible increased susceptibility to certain infections.

Although the leukocyte count varies considerably during pregnancy, usually it ranges from 5×10^9/l to 12×10^9/l. During labor and the early puerperium, it may become markedly elevated, attaining levels of 25×10^9/l or even more, how-

ever, it averages 14×10^9/l to 16×10^9/l. The cause for the marked increase is not known, but the same response occurs during and after strenuous exercise. It probably represents the reappearance of leukocytes previously shunted out of active circulation. Interestingly, increasing numbers of immune cells are also found in the uterine wall during normal pregnancy. These cells, especially mast cells, may play an important role in mediating uterine contractility.

In addition to normal variations in the leukocyte count, the distribution of cell types is altered significantly during pregnancy. Specifically, during the third trimester, the percentages of granulocytes and CD8 T lymphocytes are significantly increased along with a concomitant reduction in the percentages of CD4 T lymphocytes and monocytes. Moreover, circulating leukocytes undergo significant phenotypic changes including, for example, the upregulation of certain adhesion molecules.

Platelets

Normal pregnancy also involves changes in platelets — mostly the average platelet count was decreased slightly during pregnancy to 213×10^9/l compared with 250×10^9/l in nonpregnant control women. Decreased platelet concentrations are partially due to the effects of hemodilution. However, they also likely represent increased platelet consumption, leading to a greater proportion of younger, and therefore, larger platelets. Beginning in midpregnancy, production of thromboxane A_2, which induces platelet aggregation, progressively increases.

Hemostatic system

Normally hemostasis depends on the function of the central organs (liver, spleen, bone marrow), peripheral formations (vascular wall, blood cells, plasma factors), local systems (biologically active substances, tissue factor). Hemostasis is provided by the joint response of the vascular wall, platelets, coagulation factors and fibrinolysis.

During pregnancy the activity of all components of hemostasis increases. This is shown by increase in coagulation factors production, increased functional activity of platelets with a slight decrease in their number, content and reduced activity, antithrombin III, inhibited fibrinolysis. Fibrin is deposited on the walls of blood vessels in the uteroplacental system. These changes are compensatory and adaptive significance and due the formation of utero-placental blood flow and prevent blood loss during delivery.

Maternal blood does not mix with the blood of the fetus and the transition of substances from the mother's blood to the fetus and back is carried out by the fact that blood flow in the intervillous space, slow and maternal blood in it does not clot. In the third stage of labor when there is a detachment of the placenta from the uterine wall, violated the integrity of the blood vessels, is accompanied by loss of blood.

Normally, a woman in labor should not lose more than ***0.5 %*** of blood from the body weight.

Timely and reliablely hemostasis provide a reduction in muscle fibers of the uterus and blood clots in placental site. Contractions of the myometrium promotes compression of the veins and spiral uterine arteries. Contribute to the formation of blood clots blood clotting factors and tissue activator of the elements of the placenta in placental site. Retroplacental has enhanced blood clot formation, factors regulating this complex system are the placenta. Reliable hemostasis is achieved after the formation of dense fibrin clots firmly connectedness with the wall vessels and closing their defects. The hemostatic effect is achieved within 2–3 hours after birth.

Changes in hemostasis during pregnancy indicate an increase in the rate of blood clotting, decreased fibrinolytic activity and strengthening the structural properties of a blood clot.

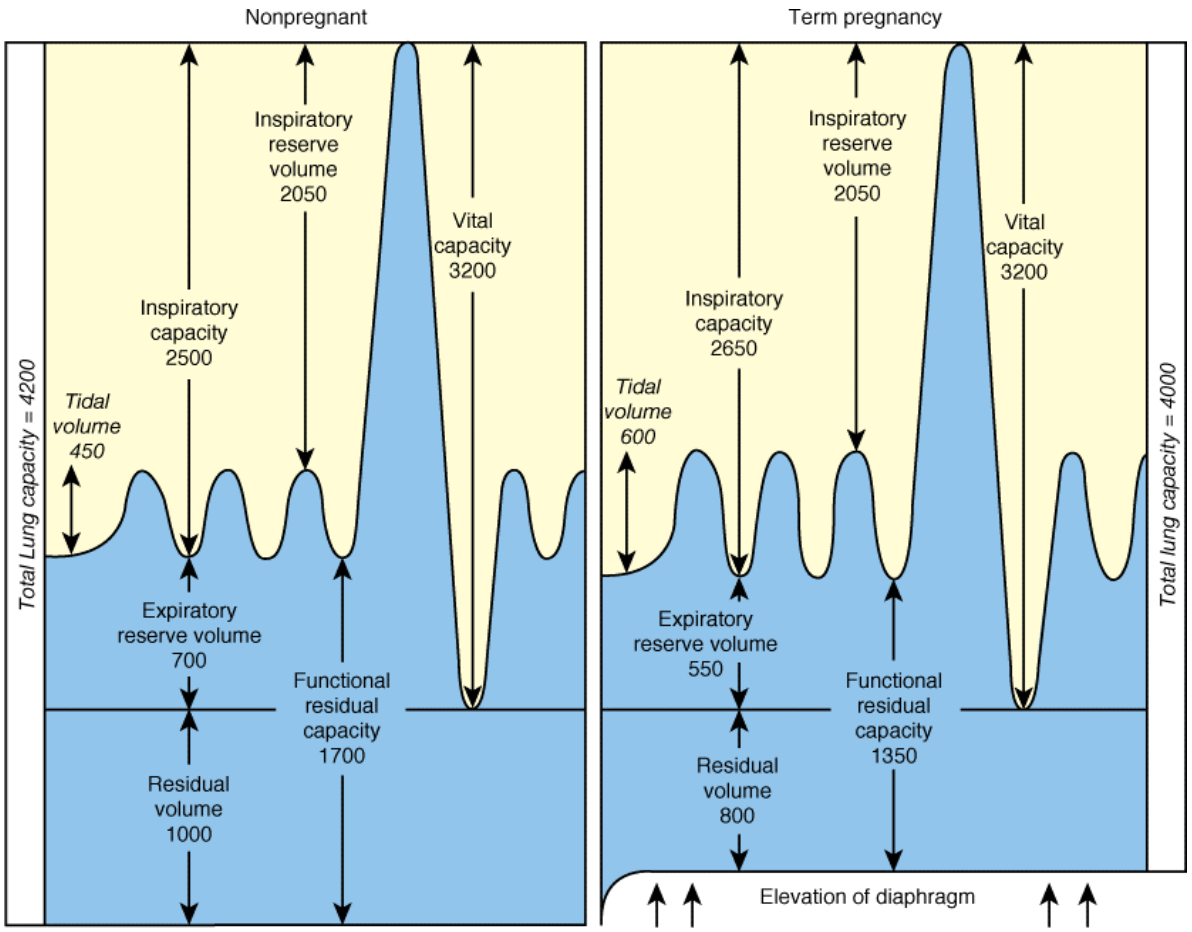
Table 1 — Changes in Measures of Hemostasis during Normal Pregnancy

Parameter	Nonpregnant	Pregnant (35–40 weeks)
Activated PTT (sec)	31.6 ± 4.9	31.9 ± 2.9
Thrombin time (sec)	18.9 ± 2.0	22.4 ± 4.1[a]
Fibrinogen (mg/dL)	256 ± 58	473 ± 72[a]
Factor VII (%)	99.3 ± 19.4	181.4 ± 48.0[a]
Factor X (%)	97.7 ± 15.4	144.5 ± 20.1[a]
Plasminogen (%)	105.5 ± 14.1	136.2 ± 19.5[a]
tPA (ng/mL)	5.7 ± 3.6	5.0 ± 1.5
Antithrombin III (%)	98.9 ± 13.2	97.5 ± 33.3
Protein C (%)	77.2 ± 12.0	62.9 ± 20.5[a]
Total Protein S (%)	75.6 ± 14.0	49.9 ± 10.2[a]

Pulmonary Changes

The respiratory rate is essentially unchanged, but *tidal volume* and *resting minute ventilation* increase significantly as pregnancy advances. The increase in minute ventilation is caused by several factors including enhanced respiratory drive primarily due to the stimulatory effects of progesterone, low expiratory reserve volume, and compensated respiratory (picture 2).

The *functional residual capacity* and the *residual volume* are decreased as a consequence of the elevated diaphragm (Fig.). *Peak expiratory flow rates* decline progressively as gestation advances. *Lung compliance* is unaffected by pregnancy, but *airway conductance* is increased and *total pulmonary resistance* reduced, possibly as a result of progesterone. The *maximum breathing capacity* and *forced* or *timed vital capacity* are not altered appreciably. It is unclear whether the critical *closing volume* — the lung volume at which airways in the dependent parts of the lung begin to close during expiration — is changed. It has been held that this is higher in pregnancy, but this is disputed. The increased oxygen requirements and perhaps the increased critical closing volume imposed by pregnancy tend to make respiratory diseases more serious during gestation.



Picture 2 — Pulmonary changes

The total of these changes is increased ventilation.
Due to deeper but not more frequent breathing.
Most likely used to help supply increased basal oxygen consumption.

<u>These can be measured using direct spirometry</u>

- Vital Capacity — increased by 100–200 mL.
- Inspiratory Capacity — increased by 300 mL.
- Expiratory Reserve Volume- decreases.
- Residual Volume — Decreases.
- Functional Residual Capacity — reduced.
- Tidal Volume — increases from 500 to 700 mL.
- Minute Ventilation- increases up to 40 %.

Immunological Functions

Pregnancy is thought to be associated with suppression of a variety of humoral and cell-mediated immunological functions to accommodate the "foreign" semiallogeneic fetal graft.

Metabolic Changes

In response to the increased demands of the rapidly growing fetus and placenta, the pregnant woman undergoes metabolic changes that are numerous and

intense. Certainly no other physiological event in postnatal life induces such profound metabolic alterations.

Basal metabolic rate increases progressively during normal pregnancy by as much as 25 percent, most of this increase in oxygen consumption can be attributed to fetal metabolic activity. If fetal body surface area is considered along with that of the mother, the predicted and observed basal metabolic rates are similar to those in nonpregnant women.

Hepatic blood flow increases substantively as does the diameter of the portal vein. Some laboratory test results of hepatic function are altered during normal pregnancy, and some would be considered abnormal for nonpregnant patients. Total *alkaline phosphatase* activity almost doubles, but much of the increase is attributable to heat-stable placental alkaline phosphatase isozymes. Serum aspartate transaminase (AST), alanine transaminase (ALT), g-glutamyl transferase (GGT), and bilirubin levels are slightly lower compared with nonpregnant.

The concentration of serum albumin decreases during pregnancy. By late pregnancy, albumin concentrations may be near 3.0 g/dL compared with approximately 4.3 g/dL in nonpregnant women. Total albumin is increased, however, because of a greater volume of distribution from plasma volume increase. There is also a slight increase in serum globulin levels.

Pregnancy-induced aminopeptidase has oxytocinase and vasopressinase activity which occasionally causes transient diabetes insipidus.

Gastrointestinal Changes

Pregnancy has little, if any, effect on gastrointestinal secretion or absorption, but it has a major effect on gastrointestinal motility because of progesterone level and enlarging uterus influence.

As pregnancy progresses, the stomach and intestines are displaced by the enlarging uterus. Consequently, the physical findings in certain diseases are altered. The appendix, for instance, is usually displaced upward and somewhat laterally as the uterus enlarges. At times, it may reach the right flank.

Endocrine Changes

Pituitary Gland During normal pregnancy, the pituitary gland enlarges by approximately 135 percent. Although it has been suggested that the increase may be sufficient to compress the optic chiasma and reduce visual fields, impaired vision due to physiological pituitary enlargement during normal pregnancy is rare. It’s more likely when these tumors are large before pregnancy — a macroadenoma is 10 mm or greater — then enlargement during pregnancy/ The maternal pituitary gland is not essential for maintenance of pregnancy. Many women have undergone hypophysectomy, completed pregnancy successfully, and undergone spontaneous labor while receiving glucocorticoids along with thyroid hormone and vasopressin.

Growth Hormone. During the first trimester, growth hormone is secreted predominantly from the maternal pituitary gland, and concentrations in serum and am-

nionic fluid are within nonpregnant values of 0.5 to 7.5 ng/mL. As early as 8 weeks, growth hormone secreted from the placenta becomes detectable and by approximately 17 weeks, the placenta is the principal source of growth hormone secretion. Maternal serum values increase slowly from approximately 3.5 ng/mL at 10 weeks to plateau after 28 weeks at approximately 14 ng/mL. Growth hormone in amnionic fluid peaks at 14 to 15 weeks and slowly declines thereafter to reach baseline values after 36 weeks.

Placental growth hormone — which differs from pituitary growth hormone by 13 amino acid residues — is secreted by syncytiotrophoblasts in a nonpulsatile fashion. The regulation and physiological effects of placental growth hormone are incompletely understood, but it appears to have some influence on fetal growth as well as the development of preeclampsia. For example, placental growth hormone is a major determinant of maternal insulin resistance after midpregnancy.

Prolactin. Maternal plasma levels of prolactin increase markedly during normal pregnancy and concentrations are usually 10-fold greater at term — about 150 ng/mL — compared with nonpregnant women. During early lactation, there are pulsatile bursts of prolactin secretion in response to suckling.

It is known is that estrogen stimulation increases the number of anterior pituitary lactotrophs and may stimulate their release of prolactin. Thyroid-releasing hormone also acts to cause an increased prolactin level in pregnant compared with nonpregnant women, but the response decreases as pregnancy advances. Serotonin also is believed to increase prolactin, and dopamine–previously known as prolactin-inhibiting factor-inhibits its secretion. The principal function of maternal prolactin is to ensure lactation. Early in pregnancy, prolactin acts to initiate DNA synthesis and mitosis of glandular epithelial cells and presecretory alveolar cells of the breast. Prolactin also increases the number of estrogen and prolactin receptors in these cells. Finally, prolactin promotes mammary alveolar cell RNA synthesis, galactopoiesis, and production of casein, lactalbumin, lactose, and lipids.

Thyroid Gland Physiological changes of pregnancy cause the thyroid gland to increase production of thyroid hormones by 40 to 100 percent to meet maternal and fetal needs. Anatomically, the thyroid gland undergoes moderate enlargement during pregnancy caused by glandular hyperplasia and increased vascularity. Beginning early in the first trimester, levels of the principal carrier protein — *thyroxine-binding globulin* — increases, reaches its zenith at about 20 weeks, and stabilizes at approximately double baseline values for the remainder of pregnancy. *Total serum thyroxine (T4)* increases sharply beginning between 6 and 9 weeks and reaches a plateau at 18 weeks. *Free serum* T_4 levels rise slightly and peak along with hCG levels, and then they return to normal. The rise in *total triiodothyronine* (T_3) is more pronounced up to 18 weeks, and thereafter, it plateaus. *Thyroid-releasing hormone (TRH)* levels are not increased during normal pregnancy, but this neurotransmitter does cross the placenta and may serve to stimulate the fetal pituitary to secrete thyrotropin.

Thyroid hormones are necessary for metabolism and adaptive reactions, affect the processes of ossification, maturation of lung tissue, mielogenezis of fetal brain. Thyroid gland of the fetus starts functioning from 12–16 weeks of pregnancy. Thyroid hormones (thyroxine and triiodothyronine) penetrate through placenta in both directions — from the mother to the fetus and the fetus from the mother, so the level of these hormones is regulated by the coordinated function of the thyroid gland mother and fetus.

Parathyroid Glands. The regulation of calcium concentration is closely interrelated to magnesium, phosphate, parathyroid hormone, vitamin D, and calcitonin physiology. Acute or chronic decreases in plasma calcium or acute decreases in magnesium stimulate the release of parathyroid hormone, whereas increases in calcium and magnesium suppress parathyroid hormone levels. The action of this hormone on bone resorption, intestinal absorption, and kidney reabsorption is to increase extracellular fluid calcium and decrease phosphate.

Parathyroid hormone plasma concentrations decrease during the first trimester and then increase progressively throughout the remainder of pregnancy. This is the result of increased plasma volume, increased glomerular filtration rate, and maternal-fetal transfer of calcium. Estrogens also appear to block the action of parathyroid hormone on bone resorption, resulting in another mechanism to increase parathyroid hormone during pregnancy. The net result of these actions is a *physiological hyperparathyroidism* of pregnancy, likely to supply the fetus with adequate calcium.

During pregnancy marked hyperactivity of the *adrenal cortex* increased levels of *glucocorticoids*. The placenta partially performs the function of the adrenal cortex, is to provide for a safe operation and increased demands for corticoids. Corticoid function of the adrenal cortex of the fetus begins after 26 weeks of pregnancy, fetal pituitary ACTH stimulated. For the synthesis of cortisol in the adrenal glands of the fetus using progesterone synthesized by the placenta.

Musculoskeletal Changes

Progressive lordosis is a characteristic feature of normal pregnancy. Compensating for the anterior position of the enlarging uterus, the lordosis shifts the center of gravity back over the lower extremities. In a recent and interesting anthropological study, this curvature and reinforcement of the lumbar vertebrae have evolved in humans to permit bipedal posture and locomotion despite up to a 31-percent increase in the maternal abdominal mass by term.

The sacroiliac, sacrococcygeal, and pubic joints have increased mobility during pregnancy. The increase in joint laxity during pregnancy does not correlate with increased maternal serum levels of estradiol, progesterone, or relaxin. Joint mobility may contribute to the alteration of maternal posture and in turn may cause discomfort in the lower back. This is especially bothersome late in pregnancy, during which time aching, numbness, and weakness also occasional-

ly are experienced in the upper extremities. This may result from the marked lordosis with anterior neck flexion and slumping of the shoulder girdle, which in turn produce traction on the ulnar and median nerves.

The bones and ligaments of the pelvis undergo remarkable adaptation during pregnancy. During pregnancy occurs normal relaxation of the pelvic joints, and particularly the symphysis pubis. Most relaxation takes place in the first half of pregnancy. However, pelvic dimensions measured by magnetic resonance imaging are not significantly different before compared with up to 3 months after delivery.

Anatomic and physiologic changes occurring during pregnancy have the potential to affect the musculoskeletal system at rest and during exercise:

- Weight gain (typically 12 kg, but nor more than 300g/week).
- Shift in center of gravity (shifted forward, posture of increased lumbar lordosis, back pain).
- Increased ligamentous laxity (related to the effects of estrogen and relaxin).

Changes in the Uterus

During the first few weeks of pregnancy, the increase of uterine size is limited principally to the anteroposterior diameter. By 12 weeks, the body of the uterus is almost globular with an average diameter of 8 cm. On bimanual examination, it feels doughy or elastic and sometimes becomes exceedingly soft. At 6 to 8 weeks' menstrual age, a firm cervix is felt which contrasts with the now softer fundus and compressible interposed softened isthmus — the *Hegar sign*. The softening at the isthmus may be so marked that the cervix and the body of the uterus seem to be separate organs.

When using a stethoscope for auscultation, the *uterine souffle* may be heard in the later months of pregnancy. This is a soft, blowing sound that is synchronous with the maternal pulse. It is produced by the passage of blood through the dilated uterine vessels and is heard most distinctly near the lower portion of the uterus. In contrast, the *funic souffle* is a sharp, whistling sound that is synchronous with the fetal pulse. It is caused by the rush of blood through the umbilical arteries and may not be heard consistently.

CHAPTER 3.
CLINICAL PRENATAL CARE

Initial Prenatal Evaluation

Prenatal care should be initiated as soon as there is a reasonable likelihood of pregnancy. The major goals are to:

1. Estimate the gestational age.
2. Define the health status of the mother and fetus.
3. Initiate a plan for continuing obstetrical care.

Typical components of the initial visit :

— history (menstrual, sexual, childbirth and secretory functions);
— physical examination;
— blood pressure (both hands)m pulse;
— maternal weight;
— body temperature;
— HIV counceling.

Special external obstetrical examination:

— mammary glands;
— fundal height;
— pelvic examination;
— sacral rhombus (Mikhaelis);
— radiocarpal index (Solovjev);
— abdominal circumference;
— fetal lie;
— presentation;
— position and type of position.

Special examination:

— per speculum;
— per vaginum;
— Pap smear screening;
— bacterioscopy from the cervical channel, fornix and urethra.

Additional examination:

— bacteriology from the cervical channel, fornix and urethra and detection for antibiotics sensivity;
— sexually transmitted diseases screening — HPV, HSV, CMV and others;
— rectovaginal examination.

Laboratory tests:

— Blood type and Rh factor.
— Full blood count.
— HIV screening.
— Syphilis serology.
— Glucose blood test.
— Blood biochemistry (bilirubin, protein, kreatinin, ALT, AST).
— Urine analysis.
— Coagulogram.

Additional laboratory tests:

— antibody screen;
— anty-phospholypid syndrome screening;
— glucose – tolerance test;
— urine Zimnitski and Nechiporenko analysis etc.

Instrumental examination:

— ECG.
— Ultrasound of the uterus and fetus.
— Cardiotocogram.
— Ultrasound of the internal organs.
— Chorion biopsy.
— Amniocentesis.

Additional instrumental examination:
— amnioscopy;
— dopplerometry of blod vessels in the uterus and in fetus;
— colposcopy.

Specialists examination:
— therapeutist (general practitioner);
— ophthalmologist;
— endocrinologist;
— dentist;
— otolaryngologist.

The initial plan for subsequent care may range from relatively infrequent routine visits to prompt hospitalization because of serious maternal or fetal disease.

There are many risk factors that can be identified and given appropriate consideration in pregnancy management. Examples of common risk factors proposed by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2007) are shown. In addition, we have lists ongoing risk factors for which consultation may be indicated. Some conditions may require the involvement of a maternal-fetal medicine subspecialist, geneticist, pediatrician, anesthesiologist, or other medical specialist in the evaluation, counseling, and care of the woman and her fetus.

Recommended Consultation for Risk Factors Identified in Early Pregnancy [a]

Asthma
Symptomatic on medication
Severe (multiple hospitalizations)
Cardiac disease
Diabetes mellitus
Drug and alcohol use
Epilepsy (on medication)
Family history of genetic problems (Down syndrome, Tay-Sachs disease, phenylketonuria)
Hemoglobinopathy (SS, SC, S-thalassemia)
Hypertension
Prior pulmonary embolus or deep vein thrombosis
Psychiatric illness

Pulmonary disease: severe obstructive or restrictive
Renal disease, chronic
Requirement for prolonged anticoagulation
Severe systemic disease
Age > 35 years at delivery
Cesarean delivery, prior classical or vertical incision
Incompetent cervix
Prior fetal structural or chromosomal abnormality
Prior neonatal death
Prior fetal death
Prior preterm delivery or preterm ruptured membranes
Prior low birthweight (<2500 g)
Second-trimester pregnancy loss
Uterine leiomyomas or malformation
Human immunodeficiency virus (HIV)
CDE (Rh) of other blood group isoimmunization (excluding ABO, Lewis)
Initial examination condylomata (extensive, covering vulva or vaginal opening)

[a] At the time of consultation, continued patient care should be determined by collaboration with the referring care provider or by transfer of care.

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List of recommended Consultation for Ongoing Risk Factors Identified during Pregnancy [a]

Drugs/alcohol use
Proteinuria (>2+ on catheterized sample, unexplained by urinary infection)
Pyelonephritis
Severe systemic disease that adversely affects pregnancy
Blood pressure elevation (diastolic BP > 90 mm Hg), no proteinuria
Fetal-growth restriction suspected
Fetal abnormality suspected by sonography
Fetal demise
Gestational age 41 weeks
Herpes, active lesion at 36 weeks
Hydramnios or oligohydramnios by sonography
Hyperemesis, persistent, beyond first trimester
Multifetal gestation
Preterm labor, threatened
Premature rupture of membranes

Vaginal bleeding >14 weeks
Abnormal Pap smear result
Anemia (hematocrit <28 percent, unresponsive to iron therapy)
Condylomata (extensive, covering labia and vaginal opening)
HIV
CDE (Rh) or other blood group isoimmunization (excluding ABO, Lewis)

[a] At the time of consultation, continued patient care should be determined by collaboration with the referring care provider or by transfer of care.

OBG = obstetrician-gynecologist; MFM = Maternal-fetal medicine specialist.

Subsequent Prenatal Visits

Subsequent prenatal visits have been traditionally scheduled at intervals of 4 weeks until 20 weeks, and then every 2 weeks until 30 weeks, and weekly thereafter. Women with complicated pregnancies often require return visits at 1- to 2-week intervals.

At each return visit, steps are taken to determine the well-being of mother and fetus. Certain information is considered especially important — an example is assessment of gestational age and accurate measurement of blood pressure. Evaluation typically includes:

Maternal

- Blood pressure — current and extent of change.
- Weight — current and amount of change.
- Symptoms–including headache, abdominal pain, nausea and vomiting, bleeding, vaginal fluid leakage, and dysuria.
- Height in centimeters of uterine fundus from symphysis and abdominal circumference.
- Vaginal examination late in pregnancy often provides valuable information to include:

Confirmation of the presenting part and its station.Clinical estimation of pelvic capacity and its general configuration.Consistency, effacement, and dilatation of the cervix.*Fetal*

- Heart rate(s).
- Size-current and rate of change.
- Amount of amnionic fluid .
- Presenting part and station (late in pregnancy).
- Activity.

Assessment of Gestational Age

This is one of the most important determinations at prenatal examinations. Precise knowledge of gestational age is important because a number of pregnan-

cy complications may develop for which optimal treatment will depend on fetal age. Fortunately, it is possible to identify gestational age with considerable precision through an appropriately timed, carefully performed clinical examination, coupled with knowledge of the time of onset of the last menstrual period.

Fundal Height

Between 20 and 34 weeks, the height of the uterine fundus measured in centimeters correlates closely with gestational age in weeks. The fundal height should be measured as the distance over the abdominal wall from the top of the symphysis pubis to the top of the fundus. *The bladder must be emptied before making the measurement.* Obesity may also distort this relationship. Unfortunately, using fundal height alone, fetal-growth restriction may be undiagnosed in up to a third of cases.

Fetal Heart Sounds

The fetal heart can first be heard in most women between 16 and 19 weeks when carefully auscultated with a standard nonamplified stethoscope. The ability to hear unamplified fetal heart sounds will depend on factors such as patient size and hearing acuity of the examiner. Herbert and co-workers (1987) reported that the fetal heart was audible by 20 weeks in 80 percent of women. By 21 weeks, audible fetal heart sounds were present in 95 percent, and by 22 weeks they were heard in all. The fetal heart rate now ranges from 110 to 160 bpm and is heard as a double sound resembling the tick of a watch under a pillow. Because the fetus moves freely in amnionic fluid, the site on the maternal abdomen where fetal heart sounds can be heard best will vary.

Instruments incorporating Doppler ultrasound instruments are often used to easily detect fetal heart action, almost always by 10.

Subsequent Laboratory Tests

If initial results were normal, most tests need not be. Fetal malformations screening may be performed at 11 to 13,6 weeks (pregnant from group of high risk — 10–12 weeks) and/or at 19 to 22 weeks, depending on the protocol selected. Serum screening for neural-tube defects is offered at 15 to 18 weeks. Hematocrit or hemoglobin determination, along with syphilis serology if it is prevalent in the population, should be repeated at 20 and to 32 weeks. Women who are D (Rh) negative and are unsensitized should have an antibody screening test repeated to 20 weeks every 4 weeks, to 30 weeks — every 2 weeks and after — every week.

Pregnancy dating

• Nagele’s rule — add 7 days to first day of last mensruation and count back 3 months.

• McDonald’s rule — fundal height = week of gestation +/- 2–4 weeks.

• First day of last menstruation plus 280 days.

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CONTENTS

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