



## **ADAPTATION OF THE BODY TO PREGNANCY**

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### **Abstract:**

The problem of complicated pregnancy, childbirth and the postpartum period is the essence of obstetric science. The study of this problem should be based on understanding the physiology of the uncomplicated course of the gestation process, on the one hand, and an approach to this problem from the standpoint of the whole organism, on the other. Pregnancy is one of the forms of life activity, and life is one of the natural phenomena. All natural phenomena are subject to the law, according to which they go through a certain cycle in their development: conception - development - formation. The last stage of this cycle is death, after which the natural phenomenon ceases to exist, merging with the environment. This law is also true for the phenomena of living nature. Life is a constant struggle with death, which is achieved by the continuous synthesis of information-rich macromolecules, the formation of cells with their complex organization, the formation of tissues and organs. The most important role in this process is given to the synthesis of protein as a substance of the most complex structure. It is proteins that play a primary role in the structure and function of the cell, being the molecular tools with the help of which genetic information is realized. In this paper, when we talk about hypertensive disorders, we mean "obstetric" hypertensive disorders, i.e. any obstetric complications.

**Keywords:** body, hypertension, insulin, pregnancy, pregravid preparation

**INTRODUCTION.** The biological meaning of pregnancy is the creation of new life. It is clear from this that when solving the problem of pregnancy, an approach is needed from the position of the distinctive feature of life: the synthesis of substances, or more precisely, from the position of metabolism.

Metabolism in the body does not occur randomly, but in strict accordance with its needs and the influence of the environment, which is the basis of adaptation. Adaptive restructuring of metabolism occurs under the influence of changes in the systems that regulate it. These include the endocrine, immune, nervous systems, the genetic, receptor, enzymatic apparatus of the cell, biologically active substances, metabolites, ions, etc. The coordinating role belongs to the integrative systems of the body: the cerebral cortex and the limbic-reticular complex, the most important component of which is the hypothalamus.

It is obvious from this that considering the problem of pregnancy from the point of view of metabolic regulation is an approach to this problem from the position of the whole organism.

Metabolism is based on biochemical reactions that occur with the use and transformation of energy. Glucose, free fatty acids, amino acids and ketone bodies can be used as energy substrates in humans.

The proportion of the energy substrates used varies in different states of the body. At rest, the main substrate is the most easily utilized glucose. When the body's

ability to absorb glucose deteriorates, for example, with insulin deficiency or with a decrease in glucose reserves (in the case of a decrease in glycogen in the liver), fatty acids acquire a greater role as an energy substrate. Along with the utilization of fatty acids, the consumption of ketone bodies increases. Their role as an alternative energy substrate increases as the use of fatty acids slows down. In critical situations, amino acids, which can be converted into glucose, are used to provide energy to the body.

The most important role in the regulation of metabolism belongs to the endocrine system. All other regulatory systems and substances take both independent and indirect (through regulation of the endocrine system) part in this process, synthesizing ATP used in various cellular functions. Thus, the state of metabolism reflects the state of all systems, tissues and organs of the whole organism and, conversely, the functions of organs and systems are in exact accordance with the state of metabolism.

Insulin is the main hormone in the regulation of metabolism. Its importance is determined in the utilization of proteins, fats, carbohydrates, minerals and energy substrates. Glucocorticoids, sex hormones, glucagon, adrenaline, prolactin, somatotrophic and thyroid hormones are counterinsular, although some of them have insulin-like action. The interaction between insulin and counter-insulin hormones ensures adaptive



changes in metabolism, affecting all functions of the body.

### **MATERIALS AND METHODS (REVIEW)**

In this article we analyzed scientific works which were done about the changes and formations of human body during pregnancy

The most important point of today's report is the following. Analysis of clinical and laboratory data reflecting the state of metabolism in unreported pregnancy reveals many similarities with the early hypoglycemic stage of insulin-independent diabetes mellitus. According to T. A. Klyushina (1977), V. G. Baranov (1983), E. Pedersen (1979), M. N. Koch et al. (1986), the state of metabolism in an unreported pregnancy is characterized by an increase in counter-insular hormones, a decrease in the secretion of insulin origin with an unfavorable level of influence on the fetus and newborn. Changes in oral and intravenous glucose tolerance tests, inhibition of the utilization of ketone-refined fatty acids and ketone bodies in the blood are taken into account. All these changes are similar to the early hypoglycemic stage of non-insulin-dependent diabetes mellitus.

For diabetes mellitus of both types, both insulin-independent and insulin-dependent, a decrease in the biological effect of insulin is characteristic. This is the main pathogenetic mechanism of this disease. In diabetes mellitus type I, a decrease in the biological effect of insulin is associated with a deficiency of the hormone, and in insulin-independent diabetes mellitus - with high insulin resistance of tissues with normal or even increased insulin content in the blood. In the first case, we are talking about absolute insulin deficiency, and in the second - about relative.

A decrease in the biological effect of insulin in diabetes mellitus leads to activation of the polyol cycle (sorbitol pathway) - an insulin-independent pathway for glucose utilization. This changes the permeability of the basal membrane of cells and the function of the lens of the eye, vascular endothelium and nervous tissue.

The clinical expression of insulin deficiency in diabetes mellitus is universal capillaropathy. Retinopathy is a reflection of this pathology. The functional stage of retinopathy in diabetes mellitus is characterized by the expansion of the venous capillary network, an increase in its permeability, microaneurysms, and pericapillary edema.

Similar changes in the microcirculatory bed have been found during physiological pregnancy and are also accompanied by an increase in blood viscosity in the venous limb of the capillary and microcirculation disorders (Shalina R.I., 1982; Orlov V.I., 1987; Repina M.M., 1987).

In diabetes mellitus, there is damage to the autonomic and somatic nerves, visceral neuropathy, impaired vascular tone, lability of pulse and blood pressure, orthostatic hypotension, and sensory impairment.

Emotional instability, lability of pulse and blood pressure, postural hypotension, decreased tone of the urinary, hepatobiliary systems and gastrointestinal tract are also typical for uncomplicated pregnancy (Sadauskas V.M., 1976; Pytel Yu.A. and Zolotorev I.I., 1980; Shekhtman M.M., 1987; Shekhtman M.M. et al., 1989).

In diabetes mellitus, the activity of red blood cells is disrupted: their lifespan decreases, hemolysis increases, deformability decreases, aggregation increases, the hemoglobin spectrum changes with an increase in the synthesis of certain fractions that have an increased affinity for oxygen - and, as a consequence, tissue hypoxia develops.

As shown by the works of T. S. Petrashenko (1984), A. A. Radionchik et al. (1987), all these features of erythrocytes are characteristic both of diabetes mellitus and of physiological pregnancy.

Thus, the decrease in the biological effect of insulin inevitably leads to the development of hypoxia, disruption of endothelial permeability and disruption of vegetative regulation. The consequence of the decrease in the biological effect of insulin in diabetes mellitus is the accumulation of under-oxidized products, ketone bodies, acidosis, and reduction of the bicarbonate buffer. According to M. M. Sapegova (1969), M. A. Bugach (1983), all this is inherent in uncomplicated pregnancy.

In diabetes mellitus, neoglucogenesis and lipolysis are activated, which is a compensatory measure to provide alternative energy substrates, and an increase in lipid peroxidation is observed. V. G. Baranov (1983), A. R. Bayants et al. (1986), R. I. Shalina et al. (1988), L. Ya. Sukanova et al. (1988) showed that all this is also characteristic of physiological pregnancy.

Lipid metabolism in uncomplicated pregnancy is characterized as atherogenic dyslipoproteinemia of types II b and IV, which are characterized by a significant increase in triglycerides, cholesterol, and very low-density lipoproteins (Menshikov V. V., 1982; Chernukha G. A., 1987). These types of dyslipoproteinemia are also characteristic of diabetes mellitus. In the third trimester of uncomplicated pregnancy, an increase in serum non-esterified fatty acids is noted, which is also characteristic of diabetes mellitus.

The hemostasis system during uncomplicated pregnancy is characterized by hypercoagulation, which



is the initial stage of chronic DIC syndrome, characteristic of diabetes mellitus.

As established by V.V. Potemkin (1986), N. V. Strizhova, V. D. Dzhaguga (1986), both conditions are characterized by activation of the kallikrein-kinin system.

The features of catecholamine metabolism in diabetes mellitus and uncomplicated pregnancy are similar. They are reduced to activation of the sympathetic-coadrenal system. There is a tendency to increase the excretion of catecholamines and their metabolites. The relative activity of individual stages of catecholamine metabolism is characterized by activation of dopamine synthesis, a decrease in the synthesis of norepinephrine and, to a greater extent, adrenaline, and a decrease in the inactivation of catecholamines along the path of formation of vanillyl-mandelic and homovanillic acids (M. M. Shekhtman, 1976). For the exchange of catecholamines in the dynamics of uncomplicated pregnancy (from the first to the third trimester) and in the dynamics of diabetes mellitus (from 5 to 15 years), a tendency towards normalization of the indices of sympathetic-adrenal activity, both quantitative and relative exchange of catecholamines, is characteristic (Bolshakova T. E., 1973; Shekhtman M. M., 1976).

The function of an organ is closely related to the state of metabolism and is its reflection.

Renal function in the first trimester of physiological pregnancy is characterized by an increase in the glomerular filtration rate and renal blood flow, which is similar to diabetic nephropathy with a preclinical stage of Kimelstiel-Wilson syndrome. As insulin deficiency progresses in the dynamics of diabetes mellitus, a decrease in these indicators is noted. Similar dynamics of the glomerular filtration rate and renal blood flow are also characteristic of uncomplicated pregnancy in the dynamics from the first to the third trimester (Shekhtman M. M. et al., 1982; Potemkin V. V., 1986). In diabetes mellitus, there is a decrease in albumin synthesis and an increase in globulin synthesis by liver cells and the reticuloendothelial system, as well as a deterioration in the excretory function of the liver. The same changes in function are characteristic of physiological pregnancy, as shown by A. G. Mazovetsky, V. K. Velikov (1986), M. N. Kochi et al. (1986).

Thus, all of the above allows us to conclude that during physiological pregnancy there is a relative insulin deficiency, progressing from the first trimester to labor. In other words, we can state that the basis of adaptation is a decrease in the biological effect of insulin, being its trigger and a factor supporting the adaptive restructuring of metabolism.

The subsequent sequence of changes in the systems regulating metabolism can be imagined as follows. The most important consequence of relative insulin deficiency is the movement of ions (sodium, potassium, chlorine, calcium, hydrogen, etc.) and hypoxia, which affects the action potential, i.e. the activity of excitable tissues: nervous and muscular. Activation of hypothalamic neurons leads to the production of neuropeptides and mediators and, consequently, changes the activity of the endocrine system. The latter, in turn, affects the state of the cell membrane and antioxidant activity (thereby controlling the action potential), as well as the concentration of secondary messengers and ATP synthesis. The amount of macroergs determines the activity of all cells in the body, including cells of the immune system (R. V. Petrov, 1983).

Looking at the problem of the body's adaptation from a different angle explains why the biological effect of insulin should be reduced. Adaptation implies a change in metabolism in accordance with the new needs of the organism, i.e. a change in the synthesis of substances either qualitatively or quantitatively. In this case, the synthesis of substances must be preceded by the breakdown of proteins, fats, carbohydrates, nucleic acids into primary biomolecules - building blocks, from which synthesis will then be carried out in accordance with the new conditions of the organism's existence. Since insulin is "responsible" for the synthesis of proteins, fats, carbohydrates, etc., their breakdown is possible only with a decrease in its biological effect.

Thus, clinical and laboratory analysis of the physiological process - pregnancy, allows us to establish that a decrease in the biological effect of insulin is the material substrate that underlies the body's adaptation to pregnancy.

The most important consequence of relative insulin deficiency for understanding the essence of the problem under consideration is hypoxia.

It is known that life activity is a continuous adaptation. Its essence lies in the restructuring of metabolism - according to the needs of the organism and the conditions of the external environment. This is reflected in general adaptation reactions. General adaptation reactions of training, activation, chronic and acute stress are known. Various general adaptation reactions develop in response to stimuli of different strength and duration. As a rule, a general adaptation reaction of training develops in response to a weak stimulus. As the effect of the previous strength continues (or with an increase in the stimulus), it turns into a general adaptation reaction of chronic or acute stress (data from Garkvi L.Kh. et al., 1979; Selye G., 1960).



Endogenous irritants that cause the development of a general adaptation reaction are hypoxia, changes in the concentration of ions, metabolites, water, etc. due to a decrease in the biological effect of insulin that occurs during adaptation. Exogenous influences only modify endogenous hypoxia and other factors. Hypoxia is minimal in the general adaptive reaction of activation - the least insulin deficiency, and in the general adaptive reaction of acute stress - the greatest. As established by L. H. Garkvi et al. (1979), general adaptive reactions develop in stages and are accompanied by characteristic changes in the activity of the cerebral cortex, hypothalamic-pituitary system, adrenal glands, immune system, hemostasis system and peripheral blood cells. Physiological pregnancy as one of the manifestations of life is also an adaptation process. For the first half of pregnancy and from the 7th day of the postpartum period, a general adaptation reaction of training is characteristic. For the second half of pregnancy and the first week of the postpartum period, a general adaptation reaction of chronic stress is characteristic. During labor, a general adaptation reaction of acute stress is observed. In the adaptation reaction of training, the stages of orientation, restructuring and training are distinguished. In the adaptation reactions of chronic (as well as acute) stress, the stages of anxiety, resistance and exhaustion are noted.

It has also been established that similar general adaptive reactions may arise with stimuli of different strength. This is due to the existence of different levels of reactivity of the organism. L. H. Garkvi et al. (1979) identified 10 such levels of reaction, which the authors called "reaction levels". The most significant difference between the "reaction levels" is the level of energy expenditure: at low "levels" they are lower, and therefore more beneficial to the organism.

Physiological processes (adaptation) and pathological ones (maladaptation) develop according to the same laws, having their own common mechanism as a basis. This common mechanism, which is inherent in the norm and pathology, is a decrease in the biological effect of insulin. What distinguishes adaptation from maladaptation is the correspondence (in the first case) and inadequacy (in the second) of the resulting restructuring of metabolism to the needs of the organism or the influences of the environment.

The uniqueness of the physiological gestational process is that it combines adaptation and maladaptation: adaptation, since this process is physiological, and maladaptation, since it occurs at high "floors" of reaction (the amount of synthesized substances, in particular hormones, increases significantly), which is

not beneficial and is not inherent in an adult healthy organism.

Using the example of the physiological gestational process, one can trace how, under the influence of an endogenous stimulus - hypoxia, general adaptive reactions arise, replacing each other. During labor, the "floor" of the response increases.

While physiological pregnancy is an adaptation process, hypertensive disorders is a manifestation of maladaptation. In recent years, the term hypertensive disorders has been used to refer to late toxicosis of pregnancy. We believe that such an interpretation of the term hypertensive disorders is too narrow and does not contribute to a better understanding of the pathophysiological mechanisms of this pregnancy complication.

By the term hypertensive disorders we mean maladaptation, i.e. any deviation from the physiological course of pregnancy: both obstetric complications and extragenital diseases that arose or worsened during the gestation process. This is hypertensive disorders in the broad sense of the term. Only obstetric complications ("obstetric hypertensive disorders") we consider as hypertensive disorders in the narrow sense of the term. Late toxicosis of pregnancy is a special case of "obstetric" hypertensive disorders.

It is known that the organism is a self-regulating system. Self-regulation is carried out due to the presence of reverse afferentation of functional systems. Pathological afferentation from the periphery of the functional system includes compensatory mechanisms and normalizes the activity of the organism.

Pathological afferentation in hypertensive disorders is hypoxia that does not correspond to the required level: it can be either more or less pronounced. More or less hypoxia corresponds to more or less relative insulin deficiency, which is not typical for uncomplicated pregnancy. The occurrence of pathological hypoxia is evidence of a "breakdown" in the systems regulating metabolism, which disrupts the normal course of the adaptation process. Disturbances in regulatory systems can occur at any level of regulation: the cortex, subcortical formations, suprasedgmental and segmental parts of the autonomic nervous system, immune, endocrine systems, enzymatic, receptor, genetic apparatus of the cell, etc.

They can be both congenital and acquired, organic or functional. As stated earlier, in response to an irritant, general adaptive reactions develop in the body. Hypoxia that does not correspond to the required one leads to the development of general adaptive reactions that are not characteristic of physiological pregnancy. Therefore, the detection of one of these reactions during the



gestation process also indicates hypertensive disorders in the broad sense of this term.

The peculiarities of these adaptation reactions can lead to both post-term pregnancy (since better microcirculation, high cAMP, predominant activation of the cerebral cortex), and to the threat of interruption (since oxytocin synthesis is increased), bleeding during childbirth (due to hypo- and isocoagulation), fetoplacental insufficiency; fetal suffering, intrauterine growth retardation, frozen pregnancy (since there is less "shielding" of the fetus, the rejection reaction is activated), abnormalities of labor (since the ratio of catecholamines characteristic of physiological pregnancy is changed); the appearance of nausea or "non-toxic" vomiting against the background of rapid weight gain in women.

The degree of expression, the rate of increase of disturbances and specific organ localization determine the clinical picture of hypertensive disorders in these adaptation reactions. With predominant expression of disturbances in the placenta, one can expect the development of fetoplacental insufficiency. The development of adaptation reactions that are not typical for the gestational age can lead to premature birth, bleeding, abnormalities of labor, and be the cause of bearing and the occurrence of early and late toxicosis of pregnancy.

Let us consider late toxicosis of pregnancy from the perspective of the whole organism, i.e. from the perspective of regulating metabolism.

The increase in insulinemia (Klyushina G. A., 1977), glucocorticoids (Bazhanova L. P. et al., 1973; Volkova N. N., 1987) and adrenaline (Arzhanova O. A., 1978; Ventskovsky B. M., 1978; Kuryleva K. A., Malykh T. A., 1978; Gazayan M. G., 1987) indicates an increase in relative insulin deficiency in late toxicosis of pregnancy. With prolonged existence of late toxicosis, a decrease in glucocorticoids (Bazhanova L. P. et al., 1973; Vakhnina D. A. et al., 1979; Palladi G. A., 1987), adrenaline is noted; the synthesis of norepinephrine predominates (Shekhtman M. M. et al., 1982). This corresponds to the stage of exhaustion of the adaptive reaction of chronic stress. Under these conditions, adrenaline, acting on  $\alpha$ -receptors, increases the release of the Hageman factor, reduces the level of platelets and plasma fibrinogen (Almazov V. A., 1983).

Other clinical and laboratory data also indicate a greater relative insulin deficiency in late toxicosis compared to physiological pregnancy. This becomes obvious when comparing two pathological conditions: late toxicosis of pregnancy and insulin-independent diabetes mellitus, its early stages, occurring with normoglycemia or hypoglycemia.

More pronounced (compared to physiological pregnancy) relative insulin deficiency in late toxicosis of pregnancy leads to significant metabolic disorders.

When the sorbitol pathway is activated, osmotically active substances accumulate in the cells: sorbitol and fructose, which leads to an increase in osmotic pressure in the cells and their edema. At the same time, electrolyte disturbances occur: sodium accumulates in the cells, and potassium is lost. Such disturbances are also characteristic of diabetes mellitus (Shekhtman M. M. et al., 1982; Mazovetsky A. G., Velikov V. K., 1986). Activation of the insulin-independent pathway of glucose utilization in the vascular endothelium (more pronounced than in physiological pregnancy) promotes further activation of the blood coagulation system. Due to a decrease in anticoagulant activity (Kopteva L.N., 1982; Ganina A.A., 1985; Sotnikova L.G. et al., 1986; Shalina R.I., Abramchenko V.A. et al., 1988), the effect of endoperoxide on platelet membranes increases. All of the above reasons underlie the progression of DIC syndrome with its transformation into subsequent stages, which is characteristic of both pathological conditions: diabetes mellitus and late toxicosis of pregnancy (Makatsaria A.D., 1981; Potemkin V.V., 1986).

In both pathological conditions (late toxicosis of pregnancy and diabetes mellitus), due to further deterioration of glucose utilization, the use of fat as an alternative energy substrate continues to increase, which will lead to increased lipid peroxidation.

Lipid peroxidation inhibits the ability of the capillary endothelium to synthesize prostacyclin, shifting the equilibrium toward thromboxane formation (Efimov A.S. et al., 1988; Shalina R.I. et al., 1988). The absence of correction of lipid peroxidation by antioxidant activity (in contrast to physiological pregnancy) leads in these conditions to damage to the lipid layer of the basal membrane, while in uncomplicated pregnancy, damage to the basal membrane is limited to the protein layer only. Thus, with severe relative insulin deficiency and hypoxia, which are observed in diabetes mellitus and late toxicosis of pregnancy, all layers of the basal membrane of cells suffer. The consequence of these disorders is a further increase in the porosity of the basal membranes (the glomerulus of the kidneys in particular). The endothelial membrane in the renal tubules is simultaneously a tubular basal membrane over a significant area. All this determines the progression of disorders of glomerular and tubular functions of the kidneys. Clinically, this is expressed in the appearance of proteinuria, which is characteristic of the proteinuric stage of Kimelstil-Wilson syndrome in diabetes mellitus and for late toxicosis of pregnancy.



The addition of hypertension with the activation of  $\alpha$ -receptors and the depletion of the renal depressor systems marks the transition to a more severe stage of late toxicosis of pregnancy, which is similar to the nephrosclerotic stage of Kimmelstiel-Wilson syndrome in diabetes mellitus.

Reflection of progressive metabolic disorder are other indicators of deterioration of glomerular and tubular function of the kidneys in late toxicosis of pregnancy; such as decreased glomerular filtration rate, increased levels of creatinine and uric acid in plasma, and impaired renal concentrating function.

In late toxicosis of pregnancy, the most significant changes occur in the kidneys, and different forms of late toxicosis are characterized by different changes in them. In biopsy of women who have suffered late toxicosis of pregnancy, the most common finding is a picture of glomerular-capillary endotheliosis: a decrease in the lumen of the capillary loops of the glomeruli due to diffuse swelling of endothelial cells, deposition in the mesangium fibrinoid material, immunoglobulins (Gunn T.N., 1982; Nikolaev A.Yu., Rogov V.A., 1989). This picture is also characteristic of different stages of diabetes mellitus (Shulutko B.I. et al., 1982).

In late toxicosis, a violation of the aldosterone-antidiuretic hormone ratio was revealed: a decrease in the first and an increase in the second hormone (Shekhtman M. M. et al., 1982). A decrease in aldosterone contributes to an uncompensated decrease in sodium-potassium ATPase, which leads to edema. An increase in the secretion of antidiuretic hormone contributes to an increase in arterial pressure. The main causes of hypertension in late toxicosis of pregnancy are an increase in the synthesis of norepinephrine, prostaglandins of class F<sub>2</sub>  $\alpha$ , the loss of potassium ions by cells and the accumulation of sodium ions in them (depolarization of the cell membrane).

The clinical picture of preeclampsia is determined by increasing ketoacidosis (nephrotic variant) and decreased glycemia. Diplopia, facial paresthesia (numbness of the lips, tongue, chin), headache, hunger, nausea, vomiting are symptoms of a hypoglycemic state in diabetes mellitus, similar to the precursors of preeclampsia (Potemkin V.V., 1986; Serkov V.N., 1989). Solar syndrome (epigastric pain), vomiting, headache, drowsiness are characteristic symptoms of ketoacidosis. Stage II in diabetes mellitus. This syndrome is also typical for preeclampsia.

Eclampsia is a hypoglycemic coma associated with ketoacidosis. Stage II. Eclampsia, like hypoglycemic coma in diabetes mellitus, is manifested by confusion, increased muscle tone, tonic and clonic convulsions, sometimes resembling an epileptic seizure; they are

characterized by dilated pupils, normal tone of the eyeballs, increased periosteal and tendon reflexes.

It is known that in case of repeated pregnancy, late toxicosis in some women is milder or does not develop. This can be explained based on the laws of adaptation of the body. Let us recall that the completeness of the biological effect of insulin depends on the sensitivity of tissues to this hormone. In case of repeated pregnancies, tissue insulin resistance is lower due to greater production of estrogens (Orlova V.G., 1984). Consequently, in case of repeated pregnancy, the biological effect of insulin is higher. This circumstance requires less production of counter-insular hormones and less compensatory hyperinsulinemia; ketonemia decreases - and therefore the possibility of developing late toxicosis of pregnancy, preeclampsia and eclampsia.

In addition, according to the law of immunological memory, the synthesis of antibodies (including blocking immunoglobulins) increases with repeated pregnancies (Petrov R.V., 1983). Consequently, even if the cause that caused the development of late toxicosis of pregnancy remains, with repeated pregnancies, blood microcirculation decreases, the degree of which determines the clinical picture of this form of hypertensive disorders. Thus, with repeated pregnancies, immunological control increases, i.e., the "reaction floor" decreases.

Implementation of adaptation at lower "response levels" is one of the body's compensation mechanisms.

Another compensatory mechanism is hypoxic training. Its essence is as follows. With each pregnancy, due to a decrease in the biological effect of insulin, hypoxia develops, aggravated by anemia of pregnant women and blood loss during childbirth. Hypoxic training increases the body's resistance, lowering it to a low "response level". However, this cannot continue indefinitely: with repeated, especially frequent births, due to the development of iron deficiency anemia, the degree of hypoxia increases so much that compensatory mechanisms prove ineffective. Compensation is disrupted, the body is transferred to higher "response levels", which are characterized by a greater degree of decrease in the physiological effect of insulin. Clinically, this is expressed in the fact that after the fourth or fifth repeated birth, the incidence of hypertensive disorders increases again (Ukybasova T.M., 1988).

For late toxicosis of pregnancy, liver damage is a natural consequence. The condition of the liver in late toxicosis of pregnancy indicates a marked decrease in the biological effect of insulin.

Late toxicosis is characterized by a decrease in the synthesis of total protein, but albumin synthesis suffers



more (Koch M.N. et al., 1986; Serov V.N. et al., 1989). This is associated with damage to the liver cell (Akunts K.B. et al., 1983), as well as with the progressive accumulation of fibrinolysis inhibitors ( $\alpha$  2-globulins). In other words, a decrease in the albumin-synthetic function of the liver is directly dependent on the degree of decrease in the biological effect of insulin and reflects the state of the hemostasis system.

A decrease in plasma albumin, as well as the activity of the sodium-potassium pump, antioxidant activity and an increase in antidiuretic hormone are the main causes of progressive edema in late toxicosis. Acute fatty hepatosis of pregnancy is a severe complication of pregnancy. Its pathogenesis becomes clearer when compared with the mechanism of development of fatty hepatosis in diabetes mellitus. Fatty hepatosis is the most common liver lesion in diabetes mellitus.

Acute fatty hepatosis of pregnancy is a form of late toxicosis of pregnancy with predominant liver damage, indicating the depletion of compensatory mechanisms: a decrease in the glucocorticoid function of the adrenal glands and antioxidant activity; significantly expressed relative insulin deficiency with a decrease in the synthesis of protein and glycogen, accompanied by the development of acute DIC syndrome, as well as a deficiency of lipocan, which makes it impossible to use fatty acids as an alternative energy substrate (data from Martynov K. A., Farber N. A., 1982; Repina M. A. et al., 1987; Shekhtman M. M., 1987).

Hypotension of the intestinal tract, bile and urinary tract, pyelorenal reflux (one of the reasons for the frequent addition of pyelonephritis), disruption of the autonomic innervation of the lungs (one of the reasons for the protracted course of bronchitis, pneumonia) - these manifestations are often seen in late toxicosis of pregnancy and are typical for diabetes mellitus.

Both pathological conditions are characterized by decreased tone and peristalsis of the stomach, atony of its cardiac and pyloric sphincters, and slowing of the evacuation function. These signs serve as a manifestation of damage to the autonomic nervous system and the microcirculatory bed of the stomach (Mazovetsky A.G., Velikov V.K., 1986; Potemkin V.V., 1986; Shekhtman M.M., 1987; Shekhtman M.M. et al., 1989).

The most common nervous system lesion in diabetes is peripheral neuropathy. It is expressed in symmetrical pain and paresthesia in the extremities, lumbar region, cramps in the calf muscles. Pain at rest is typical, especially at night, preventing sleep. These same symptoms also apply to early manifestations of late toxicosis of pregnancy. When the spinal nerves are

affected, neuritis, radiculitis, neuralgia occur. This also occurs in late toxicosis of pregnancy.

The clinical expression of relative insulin deficiency in diabetes mellitus is universal capillaropathy, which is most pronounced in the glomeruli of the kidneys, the retina of the eye, and the distal parts of the extremities. The most demonstrative changes are in the fundus, reflecting the state of microvessels in other organs and tissues. These changes, revealed in compensated diabetes mellitus type II and late toxicosis of pregnancy, are of the same type and are manifested by microaneurysms, expansion of the venous network of capillaries with an increase in their permeability and the formation of pericapillary edema; an increase in blood viscosity and the development of sludge phenomena are noted. With the addition of hypertension - spasm of arterioles, hemorrhages, thrombosis (Mazovetsky A. G., Velikov V. K., 1986; Makatsaria A. D., 1981; Mukhamedov Kh. A., 1984; Repina M. A. et al., 1987). Changes in the immune system in both pathological conditions are similar. They are expressed in the suppression of general immunity (Petrov R. V., 1983; Gavrilenko A. S. et al., 1987; Nazarov V. G., 1987; Sotnikova N. Yu. et al., 1987; Tsvetkov V. V. et al., 1987). Activation of the humoral link is noted: the synthesis of antibodies increases, the formation of immune complexes increases (Mazovetsky A. G., Velikov V. K., 1986; Potemkin V. V., 1986; Osadchaya O. V. et al., 1988), although their deposition in tissues, as well as the degree of anaphylaxis, may vary. This is due to the different degree of reduction of the biological effect of insulin in late toxicosis of pregnancy and diabetes mellitus, different "levels" of response in these pathological conditions, and also depends on the nature of compensatory mechanisms. In both pathological conditions, a decrease in T-lymphocytes and their proliferative activity, as well as depression of apoptosis, were revealed. The acid-base balance in both forms of pathology is characterized by acidosis and a decrease in the bicarbonate buffer (Sabieva M. M., 1969; Serov V. N. et al., 1989).

Insulin resistance of tissues is minimal at the beginning of pregnancy and increases in its dynamics (Potemkin V.V., 1986; Orkodashvili L.Sh., 1987). Accordingly, relative insulin deficiency progresses from the first trimester to labor. Therefore, the development of adaptive reactions of chronic or acute stress in the first trimester of pregnancy will be accompanied by ketonuria and glucosuria due to the fact that at these times, in accordance with a smaller decrease in the biological effect of insulin, the glomerular filtration rate is increased. In the later stages of pregnancy, which are characterized by greater relative insulin deficiency (and,



accordingly, a low glomerular filtration rate), the development of these adaptive reactions will be expressed differently: proteinuria, cylindruria, an increase in creatinine in the blood, but there will be no glucosuria and ketonuria.

The progression of relative insulin deficiency (hypoxia) leads to the development of a general adaptive reaction to acute stress, the clinical expression of which is eclampsia (cerebral variant), acute fatty hepatosis (liver variant), acute renal failure, hemolytic -uremic syndrome (renal variant), acute renal-hepatic failure (mixed variant).

The development of signs of intrauterine fetal distress is possible with any deviation of hypoxia in the mother's body from the required level (either greater or lesser), but with the exhaustion of both the mother's and the fetus' own compensation mechanisms. In both cases, the reaction of rejection of the "transplant" - the fetus - is activated due to the insufficiency of T-suppressors: in the first case, they are suppressed, and in the second - insufficiently activated. In both cases, the transfer of maternal immunoglobulins G through the placenta to the fetus is enhanced, causing the development of disorders in it.

**CONCLUSION.** The basis of life is adaptation to environmental conditions and the needs of the body. Physiological pregnancy as one of the forms of life activity is an adaptation process. Complicated pregnancy (hypertensive disorders) is nothing more than a violation of adaptation. Disadaptation can occur as a result of disorders in the metabolic regulation systems at any level.

The basis of adaptation is hypoxia as a result of a decrease in the biological effect of insulin. The basis of maladaptation (including hypertensive disorders) is hypoxia, which does not correspond to the needs of the body and external influences. It, being a pathological afferentation for functional systems, includes compensatory mechanisms of self-regulation, which in some cases leads to the normalization of the adaptation process.

When compensatory mechanisms are exhausted, "obstetric" hypertensive disorders develops. "Pretoxicosis" is an intermediate state when signs of deviation from the physiological course of pregnancy and activation of compensatory mechanisms are simultaneously revealed.

Adaptive restructuring is reflected by general adaptive reactions. There are four such reactions: general adaptive reaction of activation, training, chronic and acute stress. For the first half of physiological pregnancy and from the 7th day of the postpartum period, a

general adaptive reaction of training is characteristic. In the second half of pregnancy and the first week of the postpartum period, a general adaptive reaction of chronic stress is observed, and during labor, acute stress. The appearance of other general adaptive reactions that are not characteristic of this period of the gestation process may indicate the development of hypertensive disorders. The degree of expression of disorders (and primarily microcirculation and the hemostasis system), inherent in these general adaptive reactions, not typical of physiological pregnancy, and the organ localization of disorders determine the clinical picture of hypertensive disorders. Late toxicosis of pregnancy is a special case of hypertensive disorders. It is characterized by damage to various organs and systems, however, kidney damage most often comes to the fore. Multiple organ functional failure in late toxicosis of pregnancy, as in diabetes mellitus, is caused by a decrease in the biological effect of insulin that does not meet the needs of the body.

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